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AMERICAN JOURNAL OF OPHTHALMOLOGY

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THE ROLE OF EPINEPHRINE IN THE FORMATION OF THE INTRAOCULAR FLUID*

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The present investigation is an outgrowth of studies previously reported on the mechanism of formation of the intraocular fluid.[1] In these studies attention has been focused on the physiology and biochemistry of the ciliary processes. It has been shown that a continuous oxidative interaction takes place between the epithelium and the stroma of this tissue; the epithelium oxidizes and is reduced by the stroma. This oxidative interaction is made possible by two circumstances. In the first place, the epithelium contains a relative excess of enzymes capable of activating oxygen, while the stroma contains a relative excess of enzymes capable of activating metabolites.[2] Thus the epithelium is constantly preparing an excess of oxidizing agents while the stroma is constantly preparing an excess of reducing agents. In the second place, in the space between the epithelial and stroma cells there exists a number of reversibly oxidizable substances that are capable of forming a chain of linked oxidative reactions through which the excess of oxidizing agents in the epithelium and the excess of reducing agents in the stroma can interact.[3] Up to the present, three links in this redox chain have been identified; namely, the basement membrane, ascorbic acid, and glutathione. The interaction of these two tissues across the barrier that separates them generates free energy which may be utilized to do work.

It has been shown by Clark[4] and others that the essential feature of an oxidative reaction is not a gain of oxygen or a loss of hydrogen, but a transfer of electrons from the substance that is being oxidized to the substance that is being reduced—in the present instance, a transfer of electrons from the stroma to the epithelium of the ciliary processes. It follows that the primary manifestation of the energy derived from this interaction must be a transfer of ions to balance the electron transfer, either cations passing from stroma to epithelium or anions passing from epithelium to stroma or both. It has been shown that if dyes that are anions or cations are introduced into the tissue either in the living animal or supravitally, they become distributed in accordance with these electrolytic forces, cations accumulating in the epithelium, anions accumulating in the stroma, while dyes that are undissociated are indifferently distributed in both portions of the tissue.

The passage of an ionic electric current across a charged membrane is necessarily accompanied by a movement of water through the membrane: electroendosmosis. It has been shown that a membrane exists between the epithelium and stroma, that this membrane is negatively charged at physiologic pH and

*From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. This investigation was supported in part by the John and Mary Markle Foundation. Presented before the twelfth scientific meeting of the Association for Research in Ophthalmology at Cleveland, Ohio, June 3, 1941.

hence, in view of the direction of the ionic electric current, that a movement of water from stroma to epithelium is to be expected.[1] A study of the rate of regeneration of the aqueous in animals in whom the interaction between epithelium and stroma was interrupted by withdrawal of one of the links in the redox chain showed that a considerable portion of the normal water transport into the eye could be attributed to this mechanism.

The pattern of operation of the mechanism just described whereby the energy of cellular metabolism is made available for the work of water transport can properly be called a secretion, but it must be clearly understood that this does not imply the local synthesis of some characteristic chemical component of the transported fluid as, for instance, in the "secretion" of bile by the liver. Neither is it implied that this secretory activity is necessarily under the control of local vegetative nerves. On the contrary, our studies would indicate that the activity of the ciliary processes and of the choroid plexus is continuous, like that of the kidney tubules. These organs may not require any local neural start-and-stop mechanism such as is present in the salivary or lacrimal glands. This question cannot be settled *a priori*. General physiologic considerations, however, would lead one to expect that a secretory organ such as we have described would be under some sort of control by the rest of the body, irrespective of whether this control was exerted through a local neural mechanism or through a hormone produced remotely. In view of the humoral transmission of nervous excitation, the activator would in either case be expected to be a chemical substance. Already a considerable number of such activators have been identified and shown to exert a controlling influence on the secretion of various organs—for instance, acetylcholine and epinephrine for the salivary glands, histamine for gastric secretion, secretin for the pancreas, lactogenic hormone of the pituitary for the mammary gland.

The present study represents an attempt to find such a humoral activator for the secretion of the ciliary processes. It must be kept in mind that the specific function that we wished to study was the redox interaction between epithelium and stroma in the ciliary processes, and the water-transporting mechanism that is consequent upon this interaction. Vasomotor and pharmacodynamic influences upon the ciliary capillaries and osmotic forces probably determine whether or not there is available fluid to be transported, and are of paramount importance in the whole problem of intraocular-fluid exchange. From the point of view of the present study, however, these constitute merely unpleasant experimental complications to be avoided or minimized whenever possible.

The preliminary exploratory experiments that led us to concentrate our attention upon the effects of adrenalectomy may be briefly recounted. Neither atropine, eserine, nor acetylcholine administered locally or supravitally appeared to have any effect upon the functions we were studying. Cervical sympathectomy was found to cause vasodilation in the ciliary body, but had no effect upon the capacity of the tissue to transfer dyes. Epinephrine, administered supravitally, produced definite though slight changes in tissue redox potential, which will be discussed in detail below, and this was, therefore, the first drug that we encountered which appeared worth a concentrated study. Adrenalectomy was performed in the hope that these slight effects might be exaggerated.

In the first stages of this study we attempted to perform acute experiments, removing both adrenal glands of albino rabbits and examining the ciliary body shortly afterwards. The secretory

organ was sometimes found to be inactivated but the effects of the surgical procedure were so complex that many factors had to be controlled before inactivation and reactivation could be achieved regularly: (1) These animals were moribund for lack of cortin, and this was therefore administered pre- and postoperatively in large doses. (2) It was found that prolonged anesthesia (two hours or more) with urethane or barbiturates greatly decreased the capacity of the ciliary body to transfer fluid into the eye. (3) It was found that an extensive intra-abdominal operation even without touching the adrenals likewise greatly reduced the capacity of the ciliary body to transfer fluid into the eye. Neither of these last two effects was reversible by cortin or epinephrine injections nor was either attributable to a lowered blood pressure. (4) Immediately following adrenalectomy there was an enormous disturbance in the carbohydrate metabolism: First a hyperglycemia presumably due to the mobilization of glucose from the liver by small amounts of epinephrine squeezed into the circulation by the operative trauma. This was followed by a fall in blood sugar. Both the hyper- and hypoglycemic phase in the immediate post-operative period disturbed the water transport into the eye. After 24 hours the blood sugar was found stabilized at a normal or slightly subnormal level. (5) In spite of these varied difficulties, occasional experiments were encountered in which the secretory organ was found inactivated, and in which with adequate cortin and minimal surgical shock, a dramatic reactivation of the secretory organ could be achieved on administration of epinephrine.

In view of those few favorable results, the procedure was reorganized. Transperitoneal approach was used in order to obtain the best exposure, so that accessory glands would not escape notice. With this approach the removal of the left adrenal was very easy, the right much more difficult. The operation was performed in two stages, the right adrenal being removed at the first stage. Except for occasional surgical catastrophies, the animals recovered from this operation and showed no signs of deficiency. One week later, the second adrenal was removed under light ether anesthesia. The operation rarely took more than 20 minutes. Cortin was administered intramuscularly before and after the operation as follows: 2 c.c. adrenal cortex extract (Wilson & Company, Inc., Chicago) was given some minutes before the operation (in the two-stage operations only previous to the second operation); 2 c.c. was given immediately after completion of the operation; and 2 c.c. (in the later experiments 5 c.c.) was given about seven hours after the operation. The experiments on the secretory mechanism reported below were, in general, performed approximately 15 hours later, sometimes preceded by a further dose of 1½ c.c. of cortical extract. After the operation the animals were protected from severe temperature changes and given abundant sodium chloride, and in some instances glucose intramuscularly. One day after the operation they usually appeared quite frisky and the experiments reported below were generally performed at that time. We have made no study on the later effects of this operative procedure, and do not know whether the deficiency produced is permanent or transitory.

Dye transfer

It has been shown previously[1] that acid and basic dyes when introduced into the tissues of normal animals are distributed in accordance with the ionic electric current previously described, basic dyes accumulating in the epithelium, acid dyes being confined to the stroma. The following experiments were performed on adult albino rabbits whose second adre-

nal gland had been removed one or two days before, and which had received cortin injections as already outlined.

Twenty-five mg. of crystal violet chloride dissolved in 10 c.c. distilled water was injected intravenously. After two to five minutes one eye was removed under ether anesthesia or after the animal had been killed with intravenous air injection. Portions of the ciliary body and iris were prepared on glass slides for microscopic observations, as described in a previous paper, and covered with a drop of Ringer's solution. In contrast with the normal animal whose tissues in such an experiment showed a marked accumulation of the crystal violet in the epithelium, the adrenalectomized animal showed the dye at first mainly in the stroma. After a few minutes it reached an equal concentration in epithelium and stroma. Solutions of epinephrine in Ringer's solution were prepared, and a drop of such a solution was added to some of the specimens under observation, while similar drops of Ringer's solution were added to other control specimens. With concentrations of epinephrine of 10^{-6} to 10^{-7}, a prompt movement of the dye was visible, resulting in an accumulation of the dye in the epithelium and a decolorization of the stroma in 30 to 90 seconds. At times the ciliary processes appeared to shrink somewhat during this period, as if discharging fluid. No change was noted in the Ringer's-solution controls. This experiment is not successful if too long a time elapses between removal of the tissue from the animal and addition of epinephrine. The best experiments were those performed within 10 minutes.

Seventy-five to 150 mg. of sodium bromphenol blue dissolved in 10 to 20 c.c. of distilled water was injected intravenously into an adrenalectomized albino rabbit, one eye removed after two to five minutes, and the tissue prepared as before. In a normal animal the dye under these conditions remained confined to the stroma. In the adrenalectomized animal the dye was evenly distributed in both epithelium and stroma. A drop of Ringer's solution containing 10^{-7} epinephrine was added to some samples, Ringer's solution to others. A decolorization of the epithelium developed in the tissue exposed to epinephrine. The conditions for a successful experiment were the same as those with the basic dye.

These experiments show that the asymmetrical accumulation of acid and basic dyes in the tissue completely disappears after adrenalectomy and is reëstablished on addition of minute amounts of epinephrine (table 1). In the similar experiments previously reported, we have naturally been concerned with the possibility that the asymmetrical distribution of the dyes in the tissues might be due to special staining characteristics of the tissue rather than to an ionic electric current. The fact that this asymmetrical distribution of the dyes disappears on asphyxia has been a strong argument against the latter interpretation. The present findings that the asymmetry is reversibly dependent upon the presence of 10^{-7} concentration of epinephrine makes such an hypothesis completely untenable.

Redox potentials

In a previous paper[1] the technique of using redox-indicator dyes to determine the apparent redox potential of the tissues

TABLE 1

Active (secretory) distribution of charged dyes between stroma and epithelium
(Acid dyes to stroma; basic dyes to epithelium)

	Normal	Adrenalectomy	Adrenalectomy + Epinephrine $1 \cdot 10^{-7}$ supravitally
Crystal violet	+	−	+
Bromphenol blue	+	−	+

has been given in detail. The potential measured is an index of the balance between oxidation and reduction in the tissue. Thus, if the potential becomes more positive—that is, more oxidizing—it is an indication that the rate of formation in the tissue of substances capable of oxidizing the test dyes has increased, or the rate of formation in the tissue of substances capable of reducing the test dye has decreased. Since the epithelium and stroma are normally engaged in a continuous redox interchange, it follows that, if this interchange is interfered with, the potential of the epithelium should become more positive—that is, more oxidizing—while that of the stroma should become more negative; that is, more reducing. The results of experiments on normal animals, on animals following adrenalectomy (with cortin administration), and the tissue of adrenalectomized animals following the supravital administration of epinephrine, are shown in table 2. It will be noted that after adrenalectomy there is a rise in the potential of the epithelium and a fall in the potential of the stroma. When epinephrine is administered the potentials of the two tissues again approach one another. This is precisely the effect that one would expect if the interaction between the two tissues was first interrupted and then reëstablished. When epinephrine was administered, the potentials of the tissues approached each other somewhat more closely than they do normally. This phenomenon could be shown also in the administration of epinephrine to normal tissues. Evidently the dosage of epinephrine used was such as to produce more than the normal amount of interaction between the tissues. Since epinephrine is itself capable of being oxidized, its reducing power might have some effect in lowering the apparent redox potential. The molar concentration of the dyes used was, however, much greater than that of epinephrine, and mixtures in the test tube of solutions of dyes and of epinephrine in these concentrations gave no visible reduction of the dyes.

The potential in the stroma after ad-

TABLE 2

APPARENT OXIDATION REDUCTION POTENTIALS IN CILIARY BODY OF NORMAL AND ADRENALECTOMIZED RABBITS

Redox-Indicator Dye	E'_0 (Volt) at pH 7.4	Normal		Adrenalectomy		Adrenalectomy + Epinephrine 10^{-7} to 10^{-5}	
		Epithelium	Stroma	Epithelium	Stroma	Epithelium	Stroma
Orthochlorophenol-indophenol	+0.225	++++	++++	++++	++++	++++	++++
Bindschedler's green	+0.211	++++	++++	++	++++	++++	++++
Dichlorophenol-indophenol	+0.189	++++	++++	+	++++	++++	++++
Toluelene blue	+0.101	++	++++	0	++++	+++	++++
Lauth's violet	+0.050	0	++++	0	++++	0	++++
Methylene blue	+0.002	0	++++	0	++++	0	++++
Indigotrisulphonate	−0.099	0	+++		++++		0
Indigodisulphonate	−0.143	0	+				
Safranin bluish	−0.275	0	0		+		0
Apparent potential		+0.100	−0.130	+0.210	−0.255	+0.080	−0.050 (approx.)

0 No reduction
+ 1/3 reduced
++ 1/2–2/3 reduced
+++ 2/3–9/10 reduced
++++ over 9/10 reduced

renalectomy approaches that under nitrogen asphyxia, which is the same in normal and adrenalectomized animals (table 3). The small difference is attributable at least in part to aërobic oxidation of the redox-indicator dye used in these experiments. It follows that in the adrenalectomized state oxidation of the stroma has practically ceased. Since the stroma even after adrenalectomy contains large amounts of ascorbic acid and glutathione, it may be concluded that after adrenalectomy, this tissue lacks any catalyst for the autoöxidation of these substances. On the other hand, the stroma potential of normal tissue poisoned by cyanide is considerably higher,[1] and this was also found to be the case in cyanide poisoning of tissues from adrenalectomized animals to which epinephrine had been added. It follows that epinephrine provides a catalyst for the aërobic oxidation of substances in the stroma.

Since the potential of the epithelium rises on adrenalectomy and falls on administration of epinephrine, it follows that the lack of epinephrine does not inactivate the epithelial oxidases, while the presence of epinephrine provides reducing substances with which the oxidases can react. We may, therefore, conclude that epinephrine provides a link in the redox chain that connects the oxidases of the epithelium with the dehydrogenases of the stroma, and that this link lies somewhere between the epithelial oxidase and the stroma mediators. There is no evidence as to whether this link is a chemical derivation of epinephrine itself or is derived from some totally other substance that is rendered active by interaction with epinephrine.

TABLE 3

APPARENT OXIDATION REDUCTION POTENTIAL IN THE STROMA

Redox-Indicator Dye	E'_0 (Volt) at p_H 7.4	Normal[1]			Adrenalectomy		
		Aerobic	NaCN	N_2	Aerobic	NaCN	N_2
Indigo-disulphonate	−0.143	+	++++	++++			
Cresyl violet	−0.175?	0	+++	++++			
Safranin bluish	−0.275	0	0	++++	+	+	+++
Apparent potential		−0.130	−0.200	−0.290	−0.255	−0.255	−0.290

transport of water into the interior of the eye is markedly reduced. This could be shown by measuring the rate of restoration of intraocular pressure after removal of part of the aqueous. In the present instance it was to be expected that adrenalectomy and the subsequent administration of epinephrine might affect the intraocular pressure and the rate of regeneration of the intraocular fluid in three separate ways. In the first place, the interruption of redox interaction between epithelium and stroma consequent upon adrenalectomy should affect the water transfer in the same way as that previously shown to occur in vitamin-C deficiency. In the second place, the deficiency and subsequent administration of epinephrine should have profound effects both on blood pressure and on intraocular vascular tone. If, on the administration of epinephrine, the rise in blood pressure more than balances the local vasoconstriction, a rise in intraocular pressure will result and will be added to the effect on the secretory organ. If

Water transport

In experiments reported elsewhere,[2] it has been shown that when the redox interaction between epithelium and stroma is interrupted by removal of one link in the redox chain (ascorbic acid), then the

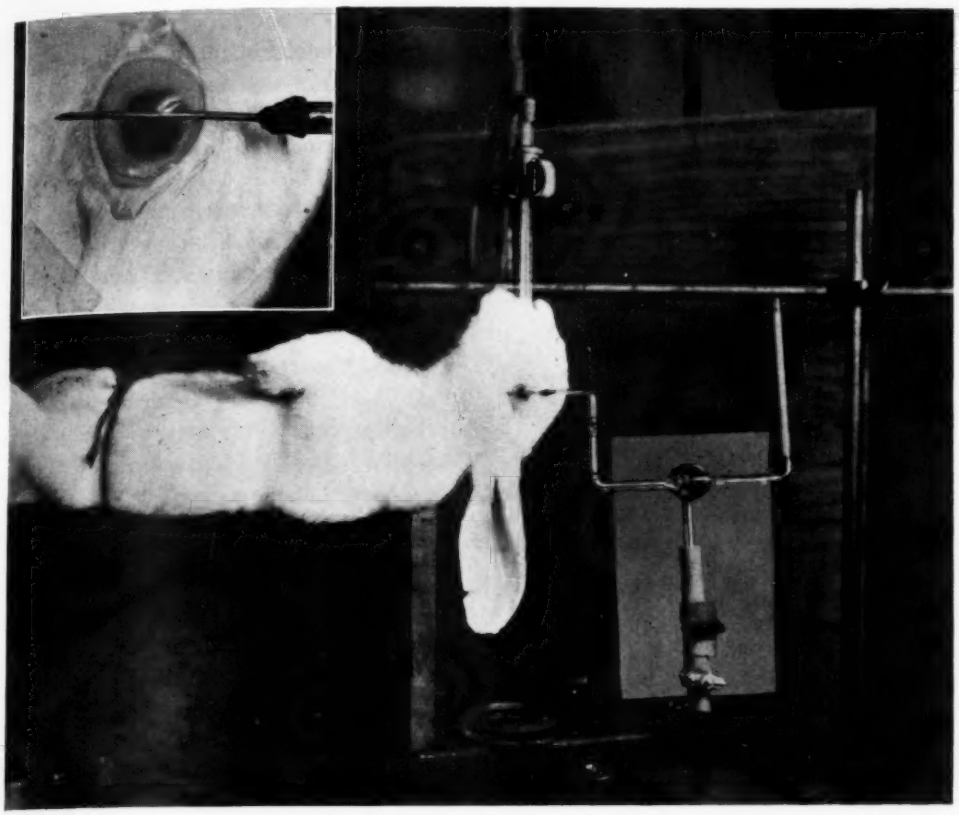
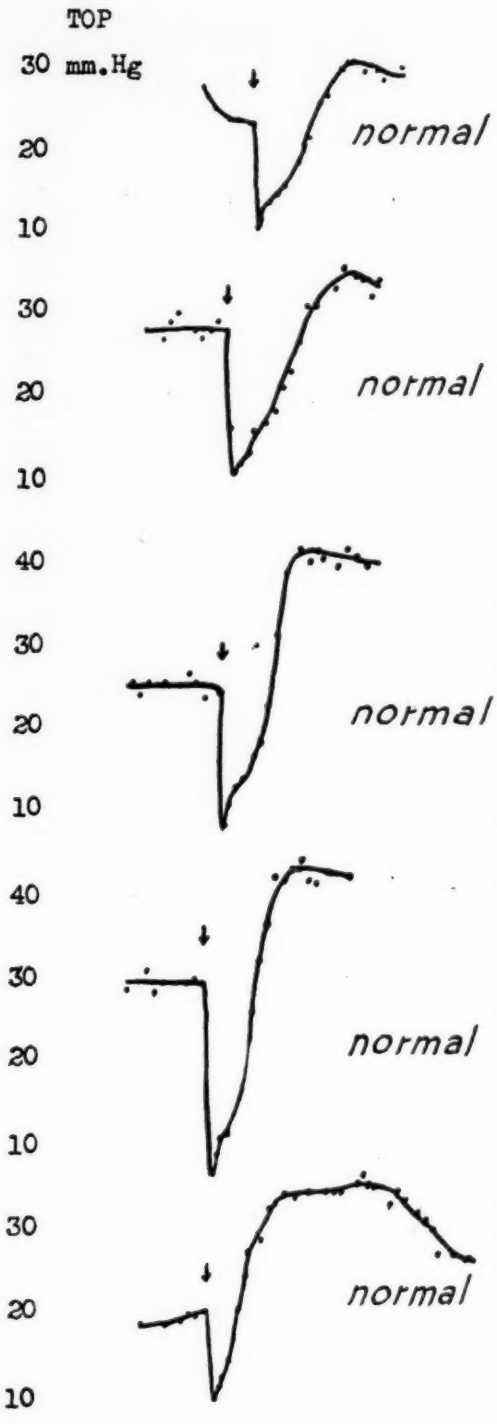


Fig. 1 (Friedenwald and Buschke). Measurement of the intraocular pressure in rabbits with compensation manometer. The closed tip of the needle has transfixed the cornea so that the needle is held steadily in place during the experiment, while a hole at the side of the needle connects the anterior chamber with the manometer.

the local vasoconstriction predominates over the rise in blood pressure, a decrease in intraocular pressure will result that will counteract the effect on the secretory organ. A third possibility to be considered is the effect of adrenalectomy (and epinephrine administration) on the osmotic pressure of the blood. Uncertainty as to the weights to be assigned to these various effects is increased in view of the uncontrollable variations in vasomotor tone at the outset of the experiments.

In spite of these difficulties of interpretation, it seemed worthwhile to measure the rate of re-formation of the aqueous in adrenalectomized animals before and after the administration of epinephrine. The experimental procedure was essentially the same as that previously used in similar experiments on vitamin-C-deficient guinea pigs.[3] Under nembutal anesthesia, with local instillation of 0.5-percent pontocaine, a compensating manometer was connected with the anterior chamber of one eye of a rabbit (fig. 1). As soon as the pressure reached a stable equilibrium, 0.1 c.c. of aqueous was withdrawn, and the subsequent course of the intraocular pressure was observed. A continuous saline drip was used to prevent drying of the cornea. A small amount of heparin dissolved in Ringer's solution was introduced into the canula of the



manometer and, by gentle changes in pressure, partially expelled into the anterior chamber at the outset of the experiment, in order to prevent clotting of the aqueous, which occurs so very readily in rabbits.

In a series of normal control experiments it was found that under the conditions of this experiment, the aqueous was very rapidly re-formed. On withdrawal of 0.1 c.c., the intraocular pressure fell to between one-third and one-half its previous level, but returned to the previous level in 4 to 10 minutes, generally overshooting the previous norm very considerably in the succeeding 10 to 20 minutes. A series of characteristic curves is shown in figure 2. Removal of the cervical sympathetic was without noticeable effect on the rate of recovery of the intraocular pressure (fig. 3).

After adrenalectomy the intraocular pressure is generally slightly lower than in normal animals. The proportionate drop in pressure on removal of 0.1 c.c. aqueous is the same as in normal animals, but the re-formation of aqueous after the withdrawal was exceedingly slow. In some experiments no measurable recovery of intraocular pressure occurred during the first 20 to 40 minutes after withdrawal. In no case was there more than 50-percent return toward the previous norm within 40 minutes after the withdrawal of aqueous (fig. 4). In general, the experiments were not prolonged beyond this period since, as noted above, the re-formation of the aqueous had been found to be adversely affected by prolonged anesthesia.

If after withdrawal of aqueous in an adrenalectomized animal, an intravenous injection is made of 0.01 to 0.1 mg. epinephrine, there follows a rise in blood

Fig. 2 (Friedenwald and Buschke). Recovery of intraocular pressure after withdrawal of 0.1 c.c. of aqueous in normal rabbits.

pressure and a rise in intraocular pressure (fig. 4b). Simultaneous measurement of the intraocular pressure and of the blood pressure in the femoral artery showed that, generally, the rise in blood pressure began before the rise in intraocular pressure, and that the intraocular pressure generally continued to rise for a short time after the blood pressure had fallen to nearly its previous level.

Control experiments were performed on normal (not adrenalectomized) rabbits in which the blood pressure had been moderately lowered by abdominal surgical shock and was, therefore, similar to that found in the adrenalectomized animals. Simultaneous measurements were made on intraocular and arterial blood pressure. Without withdrawal of aqueous, epinephrine was administered intravenously. The prompt rise induced in arterial pressure was associated with a slight but definite fall in intraocular pressure. It is evident that, under the condition of this experiment, the effect of epinephrine on the nonadrenalectomized animal is such that local vasoconstriction in the eye more than counterbalances the rise in arterial pressure, and that the net effect of epinephrine on the intraocular pressure of the nonadrenalectomized animal is small. These experiments suggest that the recovery of intraocular pressure on administration of epinephrine to the adrenalectomized animal is to be attributed mainly to an effect of epinephrine on the secretory organ. But it should be emphasized that due to the inherent complexity of factors that influence intraocular pressure (such as hydrostatic and osmotic forces), these experiments have only confirmatory validity. The weight of the argument rests

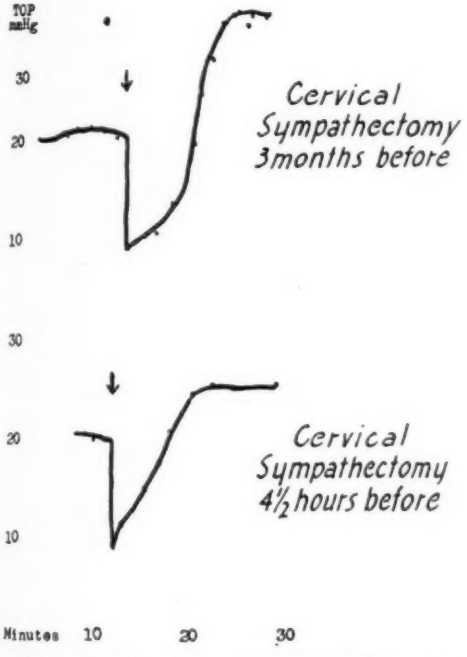


Fig. 3 (Friedenwald and Buschke). Recovery of intraocular pressure after withdrawal of 0.1 c.c. of aqueous in rabbits with cervical sympathectomy.

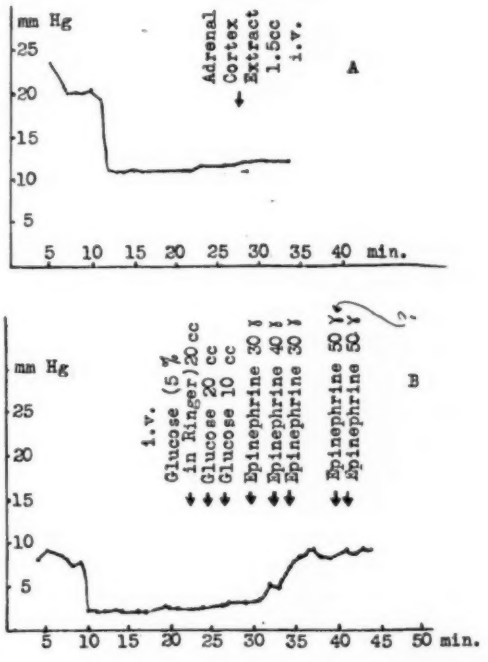


Fig. 4 (Friedenwald and Buschke). Recovery of intraocular pressure after withdrawal of 0.1 c.c. of aqueous in adrenalectomized rabbits. In A, the right adrenal had been removed one day before; the left adrenal demedullated five days before. In B, both adrenals had been removed 20 hours before.

on the experimental evidence of selective-dye transfer and tissue potentials.

Discussion

The experiments here reported demonstrate that epinephrine can activate the intercellular oxidative exchange in the ciliary body, and that the directional transport of acid and basic dyes and also probably the transport of water in this tissue is linked with this oxidative interchange. It is not possible on the basis of these experiments to conclude that epinephrine is the normal activator of this mechanism. There are many symptoms of cortin deficiency—for instance, low blood pressure and low blood sugar—which are momentarily relieved by the administration of epinephrine, and it may be argued that the inactivation which we have produced by adrenalectomy is due to cortin deficiency in spite of being relieved by epinephrine. This argument is rendered improbable, but not wholly untenable, by the fact that the inactivation persisted in spite of the administration of considerable amounts of cortin. The difficulty here lies in that there is at present no satisfactory means of assaying the degree of saturation of the animal with cortin. The mere fact that cortin is administered more than enough to enable the animal to survive, and more than enough to suppress the more obvious signs of deficiency does not prove that there is also enough for some other function. Hence there is no way at present of establishing with certainty the adequacy of any particular dosage. We have used doses of cortin that appeared to us adequate, and neither by increasing the dose nor by making observations immediately after the intravenous injection of a dose that appeared adequate for many hours could we demonstrate any effect on the inactivation of the secretory mechanism in the ciliary body. The administration of these amounts of cortin to normal nonadrenalectomized animals had no observable effect on the ciliary body. Beyond this we could not go in our efforts to exclude the possible role of cortin as activator.

Summary

The normal oxidative interaction between the epithelium and stroma of the ciliary body in rabbits is interrupted following adrenalectomy in spite of the administration of adrenal cortical hormone. Simultaneously, there is a loss in the ability of the ciliary tissues to transport acid and basic dyes in opposite directions and a marked decrease in the rate of regeneration of the intraocular fluid after anterior-chamber puncture. All three aspects of ciliary function are restored to normal by the administration either *in vivo* or supravitally of very small amounts of epinephrine.

Conclusions

Epinephrine is a potential activator of the intraocular oxidative interaction in the ciliary body. It furnishes a link in that part of the redox chain that lies between the oxidase system of the epithelium and the interstitial mediators of the stroma.

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EXPERIMENTAL TRANSPOSITION OF THE EXTRAOCULAR MUSCLES IN MONKEYS*

PRELIMINARY REPORT

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Present theories for explanation of coordinated ocular rotations postulate a relatively fixed relationship between the cerebral cortex, supranuclear gaze centers, the oculomotor nuclei, and the extraocular muscles. Accordingly it is stated that the lateral and medial recti and their respective nuclei are yoked by the action of a lateral gaze center in the pons, and are thereby enabled properly to execute the lateral rotations. In a similar manner supranuclear centers maintain control over the muscles used in convergence and upward and downward rotations. The anatomical relationship between the center and the muscles is considered fixed, but functional variability results from the intensity of the nerve impulses that arrive at the center from the cerebral cortex or from combined activity of the gaze centers.

In 1915 Marina[1] reported a return to normal rotations following the transposition of the medial and lateral recti in experimental animals. This work received little attention, but in 1936 it was confirmed by the research of Olmstead, Margutti, and Yanagisawa.[2] The results obtained by these investigators suggest that the anatomic relationship of the extraocular motor apparatus is not so fixed as had previously been believed, since following transposition the muscles apparently execute a rotation that differs from the original function. Moreover, after transposition the muscle not only takes over a new function but it becomes coordinated with its new associate in the eye that has not been operated on. However, more detailed study of the effects of single and multiple muscle transpositions is necessary in order to substantiate these results. Through further experiments, it seems possible to add to our understanding of the physiology underlying the coordinating mechanism that is responsible for smooth conjugate and disjunctive rotations.

At the present time little is known concerning the anatomic and physiologic mechanism involved in coördinated rotations. Known anatomic connections confirm the impression that vision plays a great part in the maintenance of fixation and in eye movements, but that vision is not the only factor in coördination is demonstrated by the ability of blind eyes to execute normal rotations. Volitional control of rotations by the aberrant pyramidal pathway originating in the prefrontal region is also accepted, but no coordinating function is attributed to this. Vestibular connections with the sixth nucleus and the posterior longitudinal fasciculus have been demonstrated, but functional loss of these pathways through section of the eighth nerves or destruction of the labyrinths does not disturb coördinated ocular rotations. Connections with the cerebellum and basal ganglia are entirely conjectural. Intra- and intersegmental connections exist between the various nuclei and other portions of the brain

* From the Department of Ophthalmology, College of Medicine, State University of Iowa. Portion of work being done in neuro-ophthalmic research under a grant from the American Academy of Ophthalmology and Otolaryngology. Presented at the twelfth annual meeting of the Association for Research in Ophthalmology, at Cleveland, June 3, 1941.

stem and cord by way of the posterior longitudinal fasciculus and the tectospinal pathway. Injury to these pathways interferes with coördinated rotations, but this does not prove that they constitute the coordinating mechanism. Removal of the superior colliculus without injury to the posterior longitudinal fasciculus causes no change in ocular rotations. Proprioceptive pathways from the extraocular muscles have been suggested and although Sherrington[3] and others accepted them as necessary in ocular rotations, Irvine and Ludvigh[4] deny their existence.

Previous unpublished experiments on monkeys and cats made by one of us (P. J. L.) have shown that removal of the cerebellum, section of the eighth nerves, removal of the superior colliculus, and section of the optic nerves have no effect upon coördinated ocular rotations. In one experiment in the cat it was demonstrated that removal of the cerebellum, section of the eighth nerves, and section of the optic nerves in the same animal had no effect upon the coördinated ocular rotations.

In order further to investigate some of the problems concerning ocular rotations, a series of transposition experiments was undertaken. This report considers the results of the transposition of two or more muscles of one eye.

Experimental

Technique. Monkeys (Macacus rhesus were used in all experiments. Anesthesia was obtained by intraperitoneal injection of 1.1 c.c. veterinary nembutal per five pounds of body weight. The conjunctiva and Tenon's capsule were incised and the muscles exposed. All fascial connections with the muscles were detached, particular care being used to dissect the adherent bands deep in the orbit. A muscle clamp was applied and the muscle disinserted. By means of a silk scleral suture the tendon was reattached at the insertion of the muscle with which it was being transposed. The conjunctiva was closed with a continuous silk suture.

The degree of reaction varied considerably; the animals having multiple transpositions were unable to open the eye that was operated on for three to five days because of conjunctival and palpebral edema. In only one instance was the eye lost, and this was because of infection. In several eyes a mild iridocyclitis occurred, and in one of these there was a heminecrosis of the iris, while in the others localized dilatation of the pupil occurred and persisted for several weeks. It is probable that this pupillary change was due to injury to the autonomic nerves in placing the scleral suture.

Transposition of two muscles. Transposition of the insertions of the medial and inferior recti was followed by a return of coördinated rotations in three days. On the sixth day, convergence was demonstrated. Operating on the opposite eye in the same manner resulted in return of normal rotations in three days and demonstration of convergence in five days. An additional animal was kept in the dark room after the operation and normal rotations and convergence were demonstrated on the third day. The demonstration of convergence was sometimes difficult, and since it depended entirely upon the coöperation of the monkey, knowledge of the time of its appearance would be variable.

In one monkey a considerable portion of each medial rectus was resected and the stumps were allowed to retract into the orbit. The inferior recti were then disinserted and the tendons reattached to the sclera inferior to the previous insertions of the medial recti. After three days rotations were coördinated, but there was a divergence of the optic axes. Medial rotations were well executed but somewhat restricted in extent. Attempts to demon-

strate convergence were not successful three weeks after operation.

Transposition of four muscles. Transposition of the tendons of the medial and inferior recti, and of the superior and lateral recti at one operation resulted in a return of coördinated rotations in eight days. A right hypertropia was present that increased on looking toward the side operated on, but vertical and medial rotations were well executed. There was restriction of the lateral movement of the eye that had been operated on, and rotation in the inferolateral field was absent. After 46 days the ocular rotations remained coördinated, but the right hypertropia, which increased when the eye operated on was abducted, persisted. Continuous movement of the eyes during examination suggested absence of simultanous single vision; yet when the animal was free in its cage, the ocular appearance was normal grossly.

Transposition of the insertions of the medial and inferior recti and of the superior and lateral recti was performed, and the animal placed in total darkness. Coördinated rotations were gradually regained and were considered satisfactory on the eleventh postoperative day. These animals recovered to the same degree as those that were not placed in the dark.

Transpositions of the insertions of the medial and inferior recti and of the superior and lateral recti were made, and the tendon of the superior oblique was resected. There was no recovery of ocular coördination in these animals even after three months. Movements of the eye that was operated on were in accordance with those that should result from the changed position of the transposed muscle tendons. When the normal eye looked medially the eye operated on rotated upward; while downward gaze of the normal eye was accompanied by medial movement of the eye operated on. After three months the operation was repeated on the opposite side in one animal. Following this experiment, the ocular rotations became more dissociated than previously, for now the right eye moved upward while the left eye moved down. Although convergence and divergence were present, conjugate rotations to the right or left were not executed. All movements were made in accordance with the position of the transposed tendons. Prior to the second operation, the activity of this animal was normal, but it was soon noted that, following the second operation, although the general condition was good, movements about the cage were slow and inaccurate. In grasping for the bars of the cage, the animal would frequently miss and sometimes would fall. It appeared that the animal had become disoriented. After three weeks there had been some improvement in activity but there was a great difference between the smooth and accurate activity of the cage mate and the insecure movements of the animal used for the experiment.

Discussion

The results of the experiments fall into three groups. In the first group are those animals in which only two muscles were transposed and in which recovery was complete. In the second group are those in which four muscles were transposed. Although coördinated rotations returned, there was some disturbance in the extent and type of ocular movements. This, we believe, can be explained at least in part by the rather profound interference with the mechanics of the muscles that resulted from changing the insertion of the four muscles at one time. It would account for the inability to obtain rotation of the eye operated on in the down and out position, and therefore for the tendency of the abducted eye to turn upward slightly. The third group is composed of those animals

in which the four recti were transposed, and the tendon of the superior oblique was resected. In these animals there was no return to coördinated rotations.

The experiments demonstrated that absence of vision, as obtained by placing the animal in the dark, had no appreciable effect upon the outcome of the experiments. This indicates that vision alone is not responsible for recovery of ocular coördination. It is interesting to observe that animals in the second group and no. 378 of the first group recovered coördination, although a tropia persisted and the animals appeared to have diplopia.

Apparently the effect of resection of the superior oblique after transposition of the four recti was alone responsible for the inability of the animals in the third group to regain coördination. The question arises whether this is the result of a purely mechanical disturbance. We do not believe that sufficient evidence has been obtained to give the answer at this time, but it is suggested that resecting the superior oblique so disturbed the proprioceptive mechanism of the extraocular muscles that recovery was made impossible. Further work must be done either to prove or disprove this impression.

It is natural to question whether the operations accomplished the transpositions that were attempted. Since, in all operations, particular care was taken to make the transpositions accurately, and inasmuch as rotations were incoördinated early and became coördinated later, and finally because of the results obtained in the third group of animals, it appears that transpositions were accomplished. Anatomic studies are not available on any of the animals reported, but studies of other animals operated on in initial experiments definitely show the extensive change in relationships of the insertions of the muscles.

TABLE 1

SUMMARY OF OPERATIVE PROCEDURES

Animal	Eye	Muscles Operated On	Post-operative	Recovery	Comment
377	O.D.	Med. Inf. Rec.	Light	3 days	Convergence 6 days
377	O.D.	Med. Inf. Rec.	Light	3 days	Convergence 5 days
396	O.D.	Med. Inf. Rec.	Dark	3 days	Convergence 3 days
378	O.D. O.S.	Resected Med. Transp. Inf. Rec.	Light Light	7 days	Divergent squint
389	O.D.	Med. Inf. Rec. Sup. Lat. Rec.	Light	9 days	Absent rotations down and out. Hypertropia, increased looking to right
386	O.D.	Med. Inf. Rec. Sup. Lat. Rec.	Dark	11 days	Absent rotations down and out. Hypertropia, increased looking to right
384	O.D.	Med. Inf. Rec. Sup. Lat. Rec.	Dark	11 days	Absent rotations down and out. Hypertropia, increased looking to right
380	O.D.	Med. Inf. Rec. Resected Sup. Oblique	Light	None	
397	O.D.	Med. Inf. Rec. Resected Sup. Oblique	Dark	None	
380	O.S.	Med. Inf. Rec. Resected Sup. Oblique	Light	None	Apparent loss of orientation

These preliminary experiments suggest a large series of experiments that should contribute to our knowledge and understanding of the anatomy, physiology, and pathology of the oculomotor apparatus. We do not believe that definite conclusions can be made from the work so far completed, yet we recognize the possibility of applying this method of research as a test for our present theories of oculomotor physiology.

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Discussion

Dr. Conrad Berens (New York): Did you transplant the superior oblique? If so, what was the result? The question is asked because of the surprising return of associated movements, although limited, following transplantation of the superior oblique for third-nerve paralysis with ptosis.

Dr. Leinfelder: No, I have not done any operative work on the superior oblique, except the resection of the tendon, and I think that the experiments do show that there appears to be a profound relationship between coördinated ocular rotations and the superior-oblique muscle.

However, much more work is necessary before any definite conclusions can be made, and we want to follow this work with graduated operations to see what happens when we operate on two muscles, then on two more, and finally resect the superior oblique. This may show what muscles are responsible for maintenance of coördination.

It may be that in doing a three-stage operation, we can operate on all five of the muscles and retain normal rotations. We shall be very much interested to find out whether or not that is true.

Dr. Walter B. Lancaster (Hanover): Will you repeat the description of the cat?

Dr. Leinfelder: I cut the optic nerve, the eighth nerve, and removed the cerebellum; the animal became very ugly and it lay prone in its cage.

Dr. Lancaster: I understood you to say that it did not affect the ocular rotations.

Dr. Leinfelder: No, it did not.

Dr. Lancaster: How did you test them?

Dr. Leinfelder: We observed spontaneous coördinated rotations.

Dr. Lancaster: Not random?

Dr. Leinfelder: They were random but not nystagmoid.

Dr. W. H. Marshall (Baltimore): What is the possibility that retrograde degeneration has affected the motor nuclei after superior-oblique resection?

Dr. Leinfelder: We intend to investigate that, but I do not believe that we need be concerned about degeneration of the motor nuclei, since the physiologic result shows that all of the transposed muscles are active. The physiologic result even in the animal with the abnormal rotation is

correct for the transpositions that have been made.

DR. LANCASTER: The matter of orientation interests me particularly. How did you study that in the case of monkeys?

DR. LEINFELDER: We did not study it any further than the casual observation that when the one animal was freed from the examination box and put into its cage, its activity was markedly reduced and inaccurate and that it was always much quieter in the cage than the cage mate. When jumping, it would frequently not catch the bars in the cage and would fall.

DR. LANCASTER: How many muscles did you have to cut before you affected the orientation?

DR. LEINFELDER: Five muscles in each eye were operated on.

DR. LANCASTER: As long as he had one eye he could catch the bar?

DR. LEINFELDER: That is right, but as soon as the second eye was operated on, he apparently lost all contact with what he was doing.

DR. LANCASTER: Did he show signs of closing the injured eye when he worked with one eye?

DR. LEINFELDER: Many of the monkeys would at times, but it was surprising that they did not run around the cages with one eye shut. Most of the time they had both eyes open.

DR. FRIEDENWALD (Baltimore): How much of a twist is produced by the four-muscle operation?

DR. LEINFELDER: I am not sure. We must anatomically check this to determine how much is obtained.

We attempt to minimize twist by crossing opposite pairs of muscles. While we cross the medial and inferior in one direction, which gives a twist in one direction, we try to neutralize that by crossing the superior and lateral in the other direction.

I should say offhand that there is not a great amount of twist, but that does have to be checked.

DR. E. SACHS (Detroit): Would it be possible to eliminate proprioceptive impulses from the superior oblique by the use of cocaine.

DR. LEINFELDER: We have not tried it and I doubt whether it would be of much value.

DR. SACHS: What do you expect from the diminution of the neck impulses by putting the animals in a plaster-of-Paris cast?

DR. LEINFELDER: I am not sure. Such connections must be considered along with all of the ocular motor connections from the vestibular system, the basal ganglia, possibly the cerebellum, and those that appear to originate from the superior obliquus.

DR. DERRICK VAIL (Cincinnati): How do you explain the lid ptosis?

DR. LEINFELDER: I interpreted that in part as an attempt to avoid full vision; in other words, a closure of the one eye in order to avoid diplopia. This phenomenon was not present when the animals were free in their cages.

I will say to Dr. Vail that I had not considered it very seriously.

DR. ALEXANDER E. MACDONALD (Toronto): Do you think that there is a righting reflex mechanism present, primitive or heliotropic, to explain the control of ocular movements after section of the optic nerve and the eighth nerve and removal of the cerebellum?

DR. LEINFELDER: I do not know. Our experiments are directed toward an explanation of this phenomenon.

THE PROTEIN CONTENT OF THE AQUEOUS HUMOR IN MAN*

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The present knowledge of the protein content of the aqueous humor in the more common laboratory animals may be summed up as follows: The aqueous contains proteins which are specifically identical with those found in the blood serum of the same animal. A comparison of pooled specimens of aqueous with "typical" sera of animals of the same species has shown the albumin-globulin ratios to be approximately the same in both fluids.[1] The absolute quantity of protein in the aqueous of unirritated eyes varies from 14 to 85 mg. percent in the rabbit[2] and from 15 to 55 mg. percent in the cat.[3] This amount is characteristically influenced by diuretics, certain alkaloids, experimental alterations of the sympathetic innervation, and, of course, by local irritants.[2, 4]

Based upon these facts is the widely accepted view that the proteins of the aqueous are largely or exclusively blood proteins and that their concentration in the aqueous depends chiefly upon the permeability of the blood-aqueous barrier. Conversely, the protein concentration in the aqueous has generally been considered to be a gauge of the varying state of permeability of the blood-aqueous barrier.

A year ago, before this Association, Swan and Hart[5] pointed out two important factors other than a mechanical increase in the permeability of the blood-aqueous barrier that may cause an increase in the protein content of the aqueous. "The concentration of the solids in the aqueous may be altered by variations in ocular water balance. Keys[6] found that water passes through the capillary walls more readily than do any of the serum solutes and concluded that when functional or experimental states alter the osmotic balance between blood and tissue, readjustment tends to take place by a shift of water, and only secondarily by a shift of solutes. This mechanism must be considered in the eye as a possible factor that may modify the concentration of aqueous solutes independently of changes in the permeability of the blood-aqueous barrier. Altered metabolism of the intraocular tissues may likewise alter the concentration of aqueous solutes."

Undoubtedly, both points are pertinent. If the conditions of the particular experiment are such that a systemic or local upset of the osmotic equilibrium is to be expected, one should not rely on any single native constituent of the aqueous as a criterion of ocular permeability. The distinction between increased permeability on the one hand and concentration of the aqueous by a sudden loss of water on the other can be made if *two* native constituents of the aqueous—as, for instance, the proteins and the nonprotein solids—are considered. If the change in protein content is considerably greater than the change in non-protein solids a change in the permeability of the blood-aqueous barrier has in all probability taken place. Only under very unusual conditions is it conceivable that the variations in concentration of the nonprotein solids of the aqueous due to changes in ocular water balance should amount to more than ± 15 percent. Since, with the methods now

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available, such variations of the protein content would be within the limits of the experimental error, no conclusions could be drawn from such slight variations in any case.

The second point raised by Swan and Hart, namely the possibility of an increase in the concentration of an aqueous solute being due to local metabolism and not due to increased permeability, is especially pertinent in the case of the aqueous proteins, since the concept is widely accepted that the proteins of the spinal fluid are largely the products of local cell disintegration (cytolysis). It should, however, be possible to make the distinction between these two types of protein by means of the specific immunological reactions.

One has to agree with Swan and Hart with regard to the great value for permeability studies of a foreign test substance, which when injected into the blood stream only enters the aqueous under conditions of increased permeability. Of such test substances sodium fluorescein has been used in ophthalmology for more than two decades. Its appearance in the anterior chamber after oral administration may be detected readily by illumination of the anterior chamber with ultraviolet rays and observation with the corneal microscope. Again, there is the possibility of factors other than the mechanical permeability of the barrier influencing the entrance of flourescein into the aqueous.

An almost ideal test substance for permeability studies was introduced into ophthalmology by Swan and Hart; namely, purified dahlia inulin. This substance, a nontoxic, chemically inert, nonionizable polysaccharide of large molecular weight, proved to be a very sensitive indicator of changes in the permeability of the blood-aqueous barrier produced in rabbits by instillation of cholinergic and adrenergic drugs into the conjunctival sac. With the doses of inulin used in these experiments no or very small amounts of inulin were found in the aqueous of the controls, whereas eserine, mecholyl, and epinephrine during its secondary phase caused the inulin to enter the aqueous in high concentrations that could easily be detected by microanalytical methods. The increase in the inulin concentrations in these experiments was very much greater than the increase in the concentration of nonprotein solids, so that the influence of alterations in the ocular water balance during these experiments could have been only slight.

The use of inulin for studies of the permeability of the blood-aqueous barrier in man is made difficult by the fact that very large amounts of inulin have to be injected intravenously in order to produce measurable concentrations of inulin in the aqueous. The injection of large volumes of fluid into the blood stream is apt to have manifest physiological effects upon the circulation and therefore also upon the intraocular pressure.

Another important point to be considered in this connection is the fact that the blood-aqueous barrier is not uniform anatomically and that its various portions cannot be expected to function uniformly. Thus it would seem that the permeability of the blood-aqueous barrier could and should not be defined on the basis of one foreign test substance only and that the native constituents of the aqueous humor, with the reservations pointed out by Swan and Hart, should also be considered. Of these native constituents, the proteins, if they can be shown to be largely or exclusively serum proteins, would seem a suitable test substance.

Of the determinations of the protein content of the aqueous humor in man that are reported in the literature, not more than about 50 can be considered as reasonably accurate. The specimens of aqueous in these instances were obtained from eyes

with varying clinical conditions and the results were arrived at by different methods. For these reasons the data permit only few conclusions. The basic facts with regard to the protein content of the aqueous—that is, the range of physiological variations in the same or in different individuals, the values which constitute the limits of normal, and the influence of diseases other than local inflammatory ones—are still unknown. This work was undertaken to establish some of these basic facts.

Technique

The technique of withdrawing the aqueous from the human eye by anterior chamber puncture (hereafter designated as ACP) has been described elsewhere.[7] For the determination of the protein content three methods (A, B, C) were used.

Method A. In order to determine the nature of the aqueous proteins, precipitin tests were made on a number of human-aqueous specimens, using as immune sera the sera of rabbits which, after immunization with either human serum albumin or globulin, gave positive precipitin reactions with human serum albumin or globulin in dilutions up to 1:100,000. The tests were made by the contact or layer method and with progressive dilutions of the antigen (the aqueous) in order to determine the highest dilution of antigen giving a precipitate after contact with the precipitin for one hour at room temperature.[8]

Method B was used exclusively in the earlier part of this work. It consisted of the estimation, by means of a nephelometer, of the turbidity produced by the addition to the aqueous of sodium sulphosalicylate in the presence of high concentrations of hydrochloric acid. This method, originally devised by Rona and Kleinmann,[9] was first applied (with a slight modification) to the aqueous by Franceschetti and Wieland.[10] While it is a very convenient and accurate method for comparing different dilutions of the same protein solution, it has the disadvantage that its results are influenced by the quality of the protein under examination; that is, in the case of serum dilutions, by the albumin-globulin ratio. This weakness of the method has been recognized by most investigators in this field.* Sera with the same total protein content according to protein-nitrogen determinations may, by the nephelometric method, show apparent deviations from the theoretical value of ± 25 percent. If sera with an albumin-globulin ratio of less than 1.2 are excluded (those are usually sera from patients with severe systemic diseases) the differences between the nephelometric results and those of protein-nitrogen determinations are less than ±15 percent. I have data on the albumin-globulin ratio in aqueous specimens of human eyes in which the total protein content was moderately increased (20-50 mg. percent). In these samples the albumin-globulin ratio was the same or slightly greater than in the blood of these patients (greater than 1.2 in every instance). Until now I have no data obtained by chemical methods on the albumin-globulin ratio in aquei with normal total protein content. Since the globulin molecule is considerably larger than the albumin molecule it is probable that the albumin-globulin ratio in such samples is greater than 1.2. The greatest probable difference between the nephelometric and the nitrogen-determination method in the aqueous (if the latter were applicable to the small amounts of protein present in the aqueous) would then be ±15 percent. From this it is clear that method B is best suited for the detection of changes in the total protein content

* Because of the difference in molecular size, 1 gram of serum albumin gives a stronger turbidity in the nephelometric reading than 1 gram of serum globulin.

under conditions under which the quality of the proteins is not likely to change; that is, for repeated protein determinations in the aqueous of the same individual.

In a previous communication,[7] data on the protein content of the primary and reformed aqueous obtained with method B were presented with the reservation "that for the time being the figures for the protein content of the aqueous given in this paper should be regarded as only relative and not as absolute values. . . ." The horse serum which was used as standard in that work has since been found to give, because of its high globulin content, a 25-percent weaker nephelometric reading than the average of several normal human sera with the same protein-nitrogen content. Thus the "relative figures can and in this paper have been made absolute by reducing them by 25 percent.

Method C. Looney and Walsh[11] found that in the presence of a protective colloid such as gum ghatti the size of the suspended protein particles became more uniform, whereby closer agreement between nephelometric results and protein-nitrogen determinations was obtained. For the low concentrations of protein present in the aqueous I found the nephelometer (the photometer of Pulfrich) more suitable than the photoelectric colorimeter used by Looney and Walsh. Otherwise I followed their method and found its results to check within ±15 percent of protein-nitrogen determinations on sera, the albumin-globulin ratio of which varied from 0.8 to 2.8. The method of Looney and Walsh thus represents a definite improvement over the method of Rona and Kleinmann. I am indebted to Dr. J. Friedenwald for pointing out to me that the hyaluronic acid present in the aqueous might affect the nephelometric reading. However, the addition of accurately neutralized hyaluronic acid up to concentrations of 20 mg. percent did not appreciably alter the nephelometric results.

Material

The aqueous specimens were obtained from Chinese patients seen in the clinic or hospital of the Peiping Union Medical College in Peiping, China, or from patients of the Illinois Eye and Ear Infirmary in Chicago. In the following tables, Ch stands for individuals of the Chinese race, C of the colored race, and W of the Caucasian race. Details concerning the clinical findings in the Chinese patients may be found in a previous publication.[7]

Results

The data have been arranged under four headings:

1. Does the procedure of withdrawing the aqueous alter its protein content?
2. What is the nature of these proteins?
3. To what extent does the protein content of the aqueous vary in normal eyes or in any group of patients with similar pathologic ocular conditions?
4. Are there ocular diseases other than inflammatory ones in which the protein content of the aqueous undergoes significant changes?

Effect of variations in the technique of the anterior-chamber puncture

Before the effect of variations in the technique of the ACP on the protein content of the aqueous (hereafter designated as p_1 in contradistinction to the protein content of the re-formed aqueous, p_2) could be studied, it became necessary to determine within what limits p_1 varies in the same eye without intentional variations in the technique of the ACP. Punctures were repeated on the same eye at intervals of not less than three weeks with strict adherence to the standard tech-

nique (table 1). The results of the second or third determination of p_i were not consistently lower or higher than that of the first determination. The variations of p_i observed were within ±15 percent of the average for each eye. Thus the greatest deviation from the average was no greater than the experimental error involved in determinations of such small amounts of protein. This relative constancy of p_i suggests that three weeks after an ACP the *status quo* has been restored, and that repeated punctures on the same eyes are therefore permissible for the study of the influence of variable factors upon p_i. There was no cross effect on the protein content of the aqueous of the second eye after one eye had been tapped, as cases 57520 and 55620 (table 2) show.

In studying the effect of modifications in the technique of the ACP great pains were taken to keep the following factors constant: the pressure exerted with the fixation forceps and the needle during its introduction, the length of the canal in the cornea, and the speed of the withdrawal of fluid.* Nevertheless, it happened a few times that the needle after having been introduced into the stroma of the cornea stubbornly pursued an intralamellar course and could not be made to pierce the posterior layers of the cornea. If in these instances the needle was withdrawn and reinserted in a less tangential direction, a procedure which

TABLE 1

REPEATED p_i DETERMINATIONS IN CASES OF OPTIC ATROPHY

	Date	p_i mg.%		Date	p_i mg.%
66640, Optic Atrophy of Unknown Cause, Ch, f, 22					
R.E.	11–21–38	5.6	L.E.	12–28–38	8.3
	12–12–38	7.0		2– 8–39	8.5
	1– 9–38	6.2		3– 8–39	6.9
	2–22–39	5.2		5– 5–39	8.7
	3–20–39	6.6			
	4– 5–39	6.2			
	4–13–39	5.9			
Average and range		6.1 ± 15%			8.1 ± 15%
After 3 instillations of eserine	5–16–39	7.7	After 3 instillations of eserine	3–30–39	11.9
394143, Syphilitic Optic Atrophy, Ch, f, 48					
R.E.	11–14–38	8.6	L.E.	10–24–38	9.5
	2–17–39	9.4		3– 3–39	8.5
Average and range		9.0 ± 6%			9.2 ± 7%
66556, Syphilitic Optic Atrophy, Ch, m, 50					
R.E.	12–23–38	10.7	L.E.	1– 9–39	8.9
	2– 3–39	8.5		2–17–39	10.1
	3– 3–39	11.0		5– 5–39	9.8
Average and range		10.0 ± 15%			9.6 ± 7%

* No special effort was made to determine the effect on p_i of the local anesthetic used at the ACP. Butyn was used at all ACP's done before September 15, 1936, and pontocaine thereafter. These two drugs may influence the protein content of the aqueous differently because pontocaine causes more hyperemia of the conjunctival vessels than does butyn. In case 52555, the right eye was first punctured while under the influence of butyn, and a second time nine months later while under the influence of pontocaine, the results being the same.

TABLE 2

CASES OF RETROBULBAR NEURITIS DUE TO DIETARY DEFICIENCY, CH, METHOD B

Hospital Number	Date of ACP	Eye	Technique of ACP	mg.%	Average of p_i for each Eye
56738	1– 5–37	L	complete	6.9	
	2–25–37	L	complete	7.1	
	3–19–37	L	incomplete	6.8	6.9
	4–23–37	L	complete	6.75	
	2– 1–37	R	complete	7.1	6.4
	3–30–37	R	incomplete	5.6	
56678	1–21–37	R	complete	9.3	
	4–23–37	R	complete	9.8	9.6
	2– 9–37	L	complete	10.0	
	3– 6–37	L	incomplete	8.9	9.5
364304	2– 1–37	R	complete	12.3	
	2–22–37	R	complete	10.5	11.4
	3–19–37	L	incomplete	12.2	
	5– 4–37	L	complete	12.0	
	6–14–38	L	complete	11.5	11.3
57520	2–25–37	R	complete	9.7	
	4– 1–37 (11:40 a.m.)	R	complete	6.8	8.3
	4– 1–37 (10:40 a.m.)	L	incomplete	8.3	8.6
	5–14–37	L	complete	8.9	
55620	3–30–37 (11:30 a.m.)	L	incomplete	11.9	11.9
	3–30–37 (12:30 p.m.)	R	complete	10.5	
	4–23–37		complete	11.1	11.1
	9–17–36		complete	11.7	
60810	4–26–38	L	incomplete	9.8	
	5–10–38	L	complete	10.5	10.2
	5–17–38	R	incomplete	14.0	
	5–31–38	R	complete	12.3	13.1
57962	3–15–37	R	complete	12.9	12.9
	4–13–37	L	complete	10.4	10.4
57957	4–13–37	R	complete	8.5	8.5
	3–19–37	L	complete	8.1	8.1
389674	5–12–38	R	complete	13.8	13.8
58931	5–24–38	R	complete	10.1	10.1

entailed prolonged and unduly severe pressure on the eyeball, p_i was invariably found to be higher than in uncomplicated punctures on the same eye. The results of such punctures were therefore discarded.

Special attention was given to the part played by the contact of the needle with the iris, which occurs at the end of every complete ACP, and to the possibility that the aqueous obtained by a complete ACP had been "contaminated" with small amounts of re-formed aqueous. Reference

to table 2 reveals that the protein content of the aqueous obtained by partial ACP is not consistently lower than the protein content of the aqueous obtained by complete emptying. "Contamination" of the genuine aqueous with re-formed aqueous should be more noticeable in those cases in which the re-formed aqueous contains much more protein than the original fluid. ACP's in man furnish a product that represents the genuine aqueous so far as its protein content is concerned.

The nature of the proteins of the aqueous

Precipitin tests for serum albumin and globulin following the method described (under Technique) were made on 25

TABLE 3

Comparison between the precipitin test and Method C

Initials or Hospital Number	Diagnosis	Race Sex Age	Eye	Date of ACP	Technique of ACP	Anesthesia	p_1 by method C mg%	Titer of	
								Serum Albumin	Serum Globulin
M.A.	syphilitic optic atrophy	W, M, 45	R	11–26–40	complete	pontocaine	9.6		
			R	12–28–39	complete	pontocaine		1:10	1:10
			L	1–12–40	incomplete	cocaine		1:10	1:10
			R	2–10–40	complete	cocaine		1:7.5	1:7.5
M.J.	optic atrophy due to methyl-alcohol poisoning	W, M, 32	R	12–28–40	complete	pontocaine	10.0		
			L	2–25–41	complete	pontocaine	8.0		
			R	2–16–41	complete	pontocaine		1:5	1:5
			L	3–18–41	complete	pontocaine		1:5	1:5
R.M.J.	esotropia, amblyopia	W, F, 16	R	1– 4–41	complete	pontocaine	12.0		
			R	2– 3–41	complete	pontocaine		1:5	1:5
Mc.C.	incipient senile cat.	W, M, 65	R	4–16–41	complete	pontocaine	15.4		
				4– 4–41	complete	pontocaine		1:10	1:10
C.C.	nuclear sclerosis	W, M, 62	L	1–30–41	complete	pontocaine	11.3		
			L	2–17–41	complete	pontocaine		1.5	1:2
19191	early, compens. primary glaucoma	W, F, 65	R	11– 8–40	complete	pontocaine	12.1		
			R	12–21–40	complete	pontocaine		1:10	1:10
18991	early, compens. primary glaucoma	W, M, 69	R	2– 6–41	complete	pontocaine	10.9		
			L		complete	pontocaine		1:10	1:10
B.N.	early compens. primary glaucoma	W, F, 63	R	11–27–40	complete	pontocaine	11.0		
			R	2– 6–40	complete	pontocaine		1:5	1:5

It is significant that in cases 56678 and 57520, in which the re-formed aqueous contained approximately 25 times as much protein as the original fluid, p_1 in the specimens obtained by partial emptying of the chamber did not essentially differ from p_1 in specimens obtained by complete emptying of the chamber.

The conclusions seem justifiable that (1) the touching of the iris with the needle, which occurs during an uncomplicated ACP, has no appreciable immediate effect on the protein content of the surrounding fluid, and (2) that complete specimens of aqueous taken from eyes of patients with amblyopia ex anopsia, syphilitic optic atrophy, and traumatic and other forms of primary optic atrophy. Positive reactions were obtained in the cases of all undiluted specimens, in about two thirds of the specimens when diluted 1:5, and in about one half of the specimens when diluted 1:10. If diluted 1:20, no positive reactions were observed. While the precipitin test cannot be considered a quantitative method of protein determination in the chemical sense, a positive test indicates the presence of

antigen in at least a concentration of 1:100,000 or 1 mg. percent. Since one half of the specimens gave a positive test in dilutions of the aqueous of 1:10, it would seem that they contained serum albumin and globulin each in concentrations between 1 and 10 mg. percent. The total protein content of these specimens as determined by nephelometry varied between 8 and 16 mg. percent. Thus the precipitin test and the nephelometric method indicated the presence of proteins in roughly the same concentration. In a second series the dilutions of the antigen (the aqueous) were made in smaller steps so as to determine more accurately the greatest dilution that still gave a positive test (table 3). Again the two methods indicated the presence of serum albumin and globulin in about the same quantity. Thus it appears probable that the proteins of the aqueous in human eyes in which the total protein concentration is within physiological limits consist largely of serum proteins. In addition to these the aqueous humor of normal human eyes

TABLE 4

THE CONTROL CASES

Hospital or O.P.D. number	Age Sex	Clinical Diagnosis	Vision	Date of ACP	Protein Content in mg. %
356040	48 F	L.E. central macula corneae	6/20, J3	1– 2–36	7.8
53949	19 M	R.E. cicatricial trachoma, normal bulbus	6/10, J1	12–22–36	13.3
363813	16 M	R.E. myopia, astigmatism	(−4.50 D.sph. ⌯ −3.00 D. cx 80°) 6/10, J1	5–26–38	6.2
52555	19 M	R.E. exotropia	6/6, J1	9–18–36	7.0
54030	30 M	L.E. exotropia	6/15, J1	4–18–36	11.5
58469	18 M	R.E. exotropia L.E.	6/6, J2 6/6, J1	2–18–37 3–15–37	10.3 11.5
57279	17 M	R.E. esotropia	6/6, J1	1– 5–37	10.7
52496	18 F	L.E. esotropia, amblyopia	6/50, J5	12–28–35	13.8
52633	15 M	R.E. exotropia, amblyopia	with +6.00 D.sph. ⌯ +2.00 D. cx 80° = 3/50, J8	1–11–36	8.3
52715	15 M	L.E. esotropia, amblyopia	6/60, J6	1–16–36	14.7
52782	21 M	L.E. esotropia, amblyopia	6/60, J6	1–22–36	6.4
53007	30 M	R.E. esotropia, amblyopia	6/20, J4	2– 4–36	7.0
368890	14 M	L.E. esotropia, amblyopia	finger counting at 2 m., J7	2–22–37	7.7

may contain small amounts of other proteins such as lens proteins or proteins liberated by cytolysis within the eye.

The variations of p_1

Repeated p_1 determinations on the same eye revealed variations of ± 15 percent. To what extent these variations were real or merely due to experimental errors it is impossible to say. With regard to eyes of the same individual, equality of p_1 seemed to be the rule and inequality rather the exception.

In order to study the variations of p_1 occurring in different individuals the data have been arranged according to clinical conditions (table 5). In the first three groups, the controls (table 4), the cases of retrobulbar neuritis due to dietary deficiency (table 2), and the cases of primary optic atrophy, the average and the range of variations of p_1 were practically the same. The fourth group comprised patients with proved or suspected primary compensated glaucoma in its earliest stages. Except during provocative tests the tension in these cases remained below 30 (according to the Schiötz scale of 1924) without treatment. The visual fields were normal in most of them and showed the very beginning of glaucomatous defects in the remainder. In this group the average and the range of p_1 were not essentially different from those of the first three groups.

The close agreement between these four groups seems to establish with a high degree of certainty the normal range of p_1 as lying between 5 and 16 mg. percent. The results of the few accurate p_1 determinations of previous investigators are well within that range.

TABLE 5

VARIATIONS OF p_1 ACCORDING TO CLINICAL CONDITION

Material	Number of Eyes	Average p_1 mg.%	Range of p_1 mg.%	Method of Protein Determination
Controls (Ch)	14	9.7	6.2 to 14.7	B
Cases of retrobulbar neuritis due to dietary deficiencies (Ch)	20	9.9	6.4 to 13.8	B
Cases of primary optic atrophy (Ch)	14	9.5	5.2 to 15.2	B
Early cases of primary compensated glaucoma (C and W)	20	11.8	6.8 to 16.3	C
Cases of senile cataract (Ch)	32	21.2	8.0 to 51.5	B
Cases of senile cataract (C and W)	11	26.5	11.3 to 56.0 (124.0)	C

Significant deviations from normal in noninflammatory eye diseases

A systematic study of p_1 in noninflammatory diseases of the anterior or posterior segment of the eye revealed a number of interesting facts. In this paper I shall confine myself to a discussion of the findings in senile cataract and in primary compensated glaucoma.

Table 4 contains two different groups of patients with senile cataract. All the eyes by slitlamp examination were found to be free of signs of anterior uveitis. Their tensions were taken with the tonometer at least once and found to be between 15 and 25 mm. according to the Schiötz scale of 1924. There was nothing

in the history or clinical findings of these cases that was not in every way compatible with the diagnosis of senile cataract. The p_1 values in these two groups were definitely outside the normal range, the average p_1 being 21.2 and 26.5, the upper limits 51.5 and 56.0 mg. percent, respectively. In the latter group there was one eye with hypermature cataract the aqueous of which contained 124.0 mg. percent protein. This value was not included in calculating the average.

In each cataract series 40 percent of the cases showed a nuclear type of cataract with no or only slight cortical involvement. The corresponding p_1 values tended to be within the normal range. In the remaining 60 percent of cataract cases there was extensive cortical involvement which was always associated with p_1 values above the upper limit of normal. Thus there seemed to be a definite correlation between cortical breakdown and high p_1 values.

With the exception of cases of hypermature cataract the increase in protein content of the aqueous was not great enough to be recognized by observation of the slitlamp beam in the anterior chamber (even with the aid of the colloidometer), which is probably the reason why this phenomenon has not been reported before.

What is the explanation of the high p_1 values in cortical senile cataract? Increased permeability of the blood-aqueous barrier is unlikely since Thiel[12] found that fluorescein taken by mouth did not appear in the aqueous of eyes with senile cataract and normal intraocular tension. The correlation between cortical breakdown and high p_1 suggests that some of the proteins present in the aqueous might be lens proteins, a possibility first demonstrated experimentally by Gifford, Lebensohn, and Puntenny.[13] This concept receives further support from Friedenwald's[14] experimental observation that "prolonged exposure of the capsule to the action of cataractous lens cortex increases the permeability of the capsule." In order to prove this concept it would be necessary to show that in cortical senile cataract the proteins of the aqueous are largely nonserum proteins. Unfortunately, the precipitin test is not accurate enough for such quantitative work. Further data with different methods will be required in order to settle this question.

Ever since the introduction of chemical methods into ophthalmology the protein content of the aqueous has played an important part in concepts concerning the pathogenesis of primary glaucoma. The results as reported in the literature have been conflicting.[15] Dieter[16] with a fairly reliable method found p_1 abnormally high in 17 out of 18 cases of primary glaucoma. It seemed to me that the findings in the purest form of primary glaucoma—that is, the noncongestive, completely compensated form—would be most significant. In five cases of untreated, completely compensated, noncongestive or simple glaucoma in which the tensions varied between 42 and 60, p_1 was found to be 10.8, 11.6, 11.8, 13.4, and 16.8. All of the eyes showed marked field defects, glaucomatous excavations, and anterior chambers of average depth. In other cases in which the elevation of pressure was associated with mild signs of decompensation or congestion, p_1 was found elevated as described by Troncoso, Dieter, and others. An increase in protein content thus appears to be associated not with glaucoma, but with a state of decompensation due to glaucoma. The data on the protein content presented here are in accord with the other findings (chlorides,[17] osmotic pressure[18] hyaluronic acid[19]) which indicate no essential primary differences in the chemistry of the aqueous between normal and glaucomatous eyes.

Summary

With a method based on estimation of the turbidity produced in the aqueous humor by the addition of sulphosalicylic acid the protein content of the aqueous humor (p_1) was determined on a large number of patients under varying conditions. It was found that:

1. No appreciable contamination with re-formed aqueous occurs during careful but complete aspiration of the contents of the anterior chamber.

2. Repeated p_1 determinations on the same eye showed variations of less than ± 15 percent of the average.

3. Equality of p_1 in the two eyes of the same individual seemed to be the rule, inequality the exception.

4. In four groups of cases—namely, normal controls, cases of retrobulbar neuritis due to dietary deficiency, cases of primary optic atrophy, and cases suspected of representing or proved to represent early stages of primary compensated glaucoma—p_1 varied within the same limits; that is, from 5 to 16 mg. percent.

5. This range may be considered the normal range of p_1.

6. In senile cataract with cortical breakdown p_1 is increased, probably because of diffusion of lens proteins into the anterior chamber.

7. In the pure, compensated form of primary glaucoma, p_1 is within normal limits.

My thanks are due to Dr. Helen Briggs of the Department of Biochemistry of the University of Illinois for the results of the precipitin test on aqueous specimens; to Dr. Karl Meyer of the Columbia University College of Physicians and Surgeons for supplying the hyaluronic acid prepared according to his own method; to Drs. C. K. Lin and A. H. Luo of the Department of Ophthalmology, The Peiping Union Medical College, for obtaining by ACP innumerable specimens of human aqueous humor; and to all my colleagues mentioned herein for their advice during this study.

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HISTOLOGIC EYE FINDINGS IN ARACHNODACTYLY

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Although many cases of arachnodactyly have been reported, I have found in the literature no description of the histologic findings in an eye in such a case. Zentmayer,[1] in 1935, said: "So far as I know there has been no histologic study of the eye in a case of arachnodactyly."

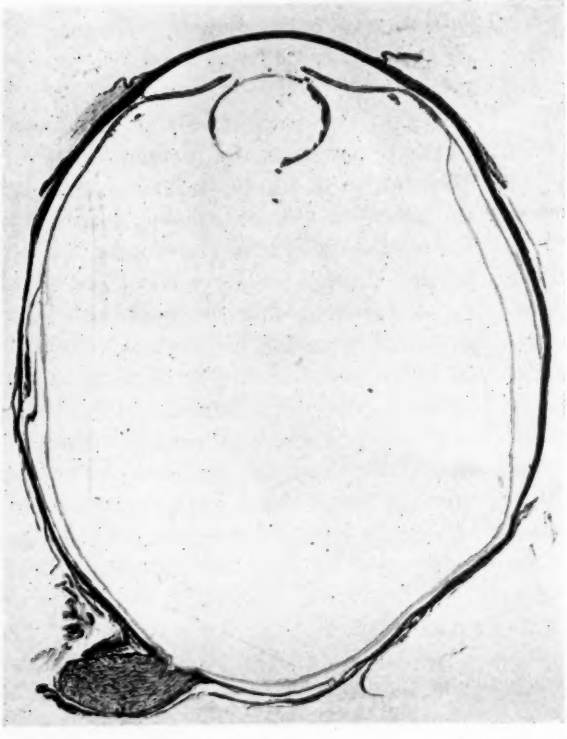

Fig. 1 (Theobald). The eye from a 2½-year-old colored child who had arachnodactyly. It measured 26.5 by 26 by 33 mm. Note incomplete separation of chamber angle, saucerlike iris, rounded lens.

CASE REPORT

The case reported here concerns a colored child, aged 27 months. This child was born with the peculiar findings of arachnodactyly, and had, at intervals since its birth, been under the care of Dr. Alwin C. Rambar.* The eyes had been examined on October 8, 1935, at Michael Reese Hospital, in Dr. Harry Gradle's clinic, by Drs. Meyer and Zekman. They found that megalocornea was present in each eye. The pupils were miotic; 2-percent atropine and 1-percent neosynephrine were used without success. Iridodonesis was slight but noticeable. The lens was dislocated upward and inward, and donesis was slight. The media were clear, and the fundi showed no abnormality. Tactile tension was normal. Because of an acute exanthema the child was moved to Cook County Hospital, where it died (1936).

The enucleated eye was given to me by Dr. Richard Jaffe, the pathologist, who had permission from the parents to remove it at autopsy.

The eye measured 26.5 mm. horizontally, 26 mm. vertically, and 33 mm. anteroposteriorly. The cornea measured 12.5 mm. horizontally and 12 mm. vertically. On the nasal side, the surface distance between the cornea and the optic nerve was 29 mm., and on the temporal side it was 45 mm. (fig. 1).

The distance from the limbus to the

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* Read before the American Ophthalmological Society at Hot Springs, Virginia, June 3-5, 1940.

[1] Zentmayer, William, discussing Burch's paper, "Association of ectopia lentis with arachnodactyly." Arch. of Ophth., N.S., 1936, v. 15, p. 676.

* For full history and preliminary eye findings see: Alwin C. Rambar, M.D., and Edward J. Denenholz, M.D.: "Arachnodactyly, report of a case with autopsy, including histologic examination of eye," Journal of Pediatrics, 1939, v. 16, no. 6, pp. 844-852.

center of the insertion of each rectus muscle was: superior rectus, 11 mm.; internal rectus, 8 mm.; inferior rectus, 8.6 mm.; and external rectus, 8.9 mm. The anterior border of the superior oblique from the limbus was 18 mm.; the width of insertion of the inferior oblique was 14 mm. Between the inferior oblique and the external-rectus muscle was an accessory inferior-oblique muscle whose insertion width was 6 mm.

The anterior chamber was of varying depths. The pupil was 3 mm. wide.

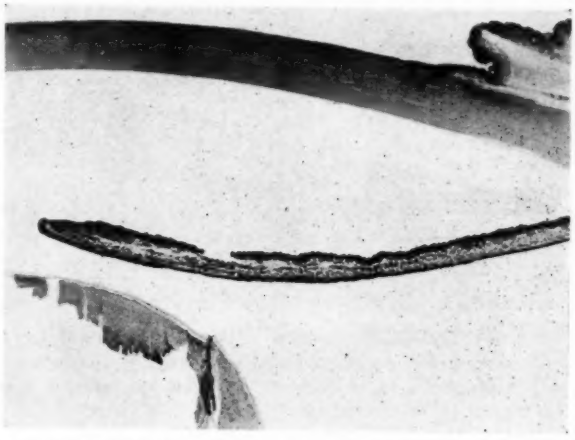

Fig. 2 (Theobald). Sections of iris showing the sphincter of the pupil and crypts of Fuchs.

Superior and inferior callots were made. The vitreous was clear, and part of it was lost on section. Vitreous lined the entire bowl. The lens was *in situ:* there was no apparent dislocation. The disc resembled a shallow saucer.

The eye was embedded in celloidin and serial sections were made.

Microscopic Examination. For the most part the cornea was covered by a single layer of cuboidal cells; near the limbus the epithelium thickened to three and four cells. The corneoscleral coat was thin, the widest measurement being 0.5 mm. at the limbus. The limbal vessels were wide. The canal of Schlemm was a narrow slit and, as was to be expected, the diameter varied from section to section. The canal was broader on the temporal side. The corneoscleral trabeculae showed openings both from the anterior chamber and into the canal of Schlemm. A congenital abnormality persisted in the chamber angles—there was incomplete separation between the iris and the trabeculum. This was more marked on the nasal side, where the trabeculae were less distinct. The anterior chamber was of varying depth. The iris varied in thickness and bowed backward, the pupillary margin and the root being nearest to the cornea. The stroma was heavy with pigmented cells. The anterior layer was composed of several layers of pigmented cells with round or oval nuclei. The stroma beneath contained heavily pigmented chromatophores, whose processes, for the most part, took a radial course. Serial sections showed Fuchs's crypts.

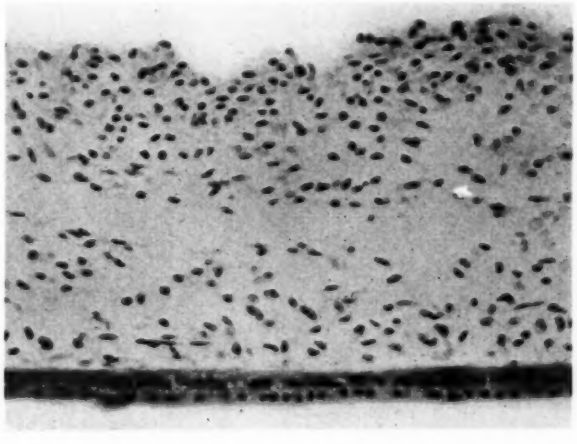

Fig. 3 (Theobald). A depigmented section of the iris showing cell structure; also absence of the dilator muscle.

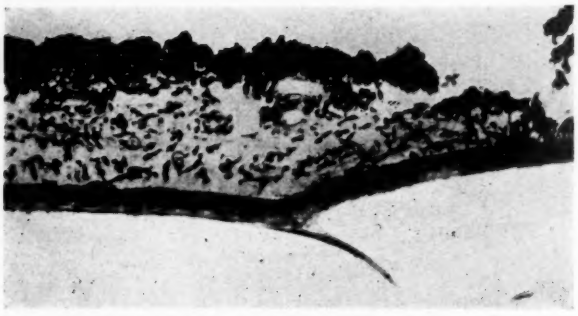

Fig. 4 (Theobald). Section of peripheral part of the iris showing the pigmented and unpigmented epithelium with a fragment of suspensory ligament extending from the unpigmented epithelium.

The iris disclosed no folds; the irregularity of the anterior surface was due to heaped-up cells. The sphincter pupillae (fig. 2) was well developed, almost 2 mm. wide, and lay immediately on the pigment epithelium. The dilator of the pupil was not formed. Over the pigment epithelium there was a homogeneous, pink-staining substance. The pars iridis retinae was interesting in that the pigmentation of its posterior layer ceased half way between the pupillary margin of the iris and the base of the ciliary processes (fig. 3). Serial sections showed ciliary processes extending from the ciliary portion of the iris. From the unpigmented epithelium on the posterior iris surface fibers were found that were similar to those of the suspensory ligament of the lens, but were of greater diameter (fig. 4).

The ciliary body was flat and long, and there was a great scarcity of circular fibers. The ciliary processes were small and few in number.

The choroid was thin; anterior to the equator several layers of vessels were seen; posteriorly, the choroid was a fine strand with only one or two layers of vessels.

The pigment epithelium beneath the retina was absent in some places, but this may have been an artifact due to tearing of the sections. Anteriorly, the retina was stretched; behind the equator the retinal layers were well differentiated. Although the sections through the macula were not perfect, the development was well shown.

The optic disc and nerve appeared to be normal; there was a large temporal conus or crescent (fig. 5).

The lens was displaced 0.5 to 1.5 mm. behind the iris. The zonular fibers were wavy (fig. 6). The lens measured 6 mm. equatorially and 4.5 mm. in the anteroposterior diameter. Most of the lens fibers fell out during sectioning, but the remaining ones appeared to be normal.

The striking thing about this eye was its size—it was truly a megaloglobus. According to Ida Mann, the size of the mesodermal elements is determined by the presence of the optic vesicle. The optic vesicle develops at the end of the fourth week. During the third month, the organogenetic period, the mesodermal eye tissues are differentiated into choroid, sclera, extrinsic muscles, conjunctiva, lids, and orbit. All of these tissues were present, but, after the fourth fetal week, the optic vesicle was stimulated to an immense growth and the mesodermal elements kept pace with it.

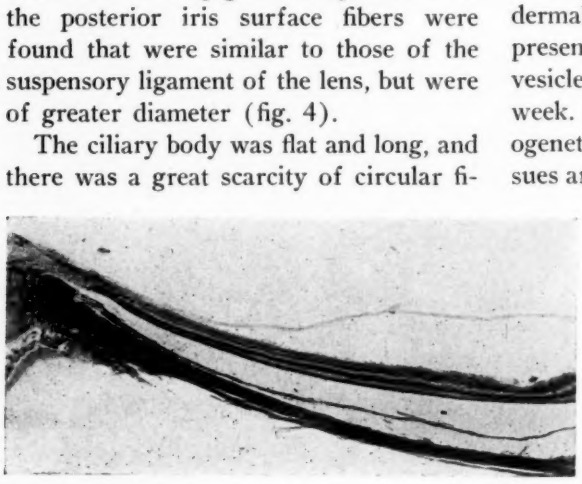

Fig. 5 (Theobald). Showing the temporal conus and macular region.

In some of the tissues an arrest of development or differentiation occurred between the fifth and seventh months. The parts af-

fected by this arrest were: (1) the dilator pupillae; (2) the posterior layer of the pars iridis retinae; (3) the tissues of the anterior-chamber angle; (4) the circular muscle of the ciliary body; (5) the suspensory ligament of the lens.

1. Although the sphincter of the pupil begins to develop at the fourth fetal month, the dilator pupillae forms during the sixth month. As has been stated, no dilator fibers could be discerned. This absence of the dilator fibers accounts for the miosis which is a frequent manifestation in arachnodactyly. Holt and Berner, in 1923, found, on histologic examination of a congenitally miotic eye, that when the dilator muscle is absent, the iris stroma is replaced by a tissue having an embryologic mucoid character. In the sections in this case this was seen as a pink-staining substance adjacent to the ectodermal pigment cells.

2. The posterior layer of the pars iridis retinae differentiates into cubical cells by the end of the fifth month. Pigmentation of these cells begins at the pupillary margin, and from the third to the seventh month progresses slowly to the base of the ciliary body. In this eye the pigmentation of these cells ceased when only half of the distance had been covered. The arrest of the pigmentation may have occurred during the fifth or sixth month.

3. The angle of the anterior chamber should be posterior to the canal of Schlemm at the seventh month, and in this eye it was definitely anterior to it. This, too, indicates an arrest of differentiation at about or during the sixth month.

4. The circular muscles of the ciliary body appear during the sixth month; in this eye only a few bundles were seen.

5. The zonular fibers are formed in from the third to the sixth months; in this eye they were very long and wavy, allowing the lens to become almost spherical.

After differentiation in these tissues was arrested, the maturing process of the eye proceeded, as was evidenced by the development of the uveal pigment and the differentiation of the macula which occurs after birth.

Fig. 6 (Theobald). The curved fibers of the suspensory ligament of the lens.

The findings in this eye show that two separate influences were responsible for the condition. First, after the fourth week, an excitant caused the gigantic growth of the optic vesicle, with which the development of the mesodermal tissues kept pace. Second (at the sixth month), a depressant

caused the arrest of development in both ectodermal and mesodermal tissues.

Marfan described this singular congenital anomaly of the skeleton which is characterized by marked elongation and a certain slenderizing of the bones of the arms and legs. He presented the first case of this malformation to the Medical Societies of the Hospitals of Paris on the 28th of February, 1896. He proposed to call it dolichostenomelia (from the Greek, δολιχός, long; στενός, narrow; μέλος, limb). At this presentation he spoke of the very long, thin emaciated fingers as "spider fingers," a phrase that so impressed Dr. Achard that he later suggested that the condition be termed arachnodactyly. Marfan agreed that this term was picturesque, but believed that it was less exact than his own term. Later on he shortened the first name to dolichomelia, but stated that he did not consider that it was any more exact than arachnodactyly. The condition later was known as the syndrome of Marfan, which designation still remains.

At first the malformation was regarded as extremely rare, but in 1938 Marfan found that 150 cases had been reported in the literature. Many of these had been discovered by ophthalmologists, who found eye conditions in more than 50 percent of the cases. The most frequent eye defects are megalocornea, megaloglobus, miosis, and ectopia lentis. Other eye complications listed are coloboma of the lens, lens opacities, iridodonesis, persistent pupillary-membrane myopia. Many interesting papers concerning the clinical aspects and findings have been written. I refer you especially to those listed in the bibliography.

Concerning the hereditary character of this syndrome, there are varying opinions. Marfan found that the condition was both hereditary and familial. He quoted Weve as finding it almost always hereditary and familial. Ormond (1930) asserted that the association of ectopia lentis with arachnodactyly is seldom a hereditary condition, but that in the few sporadic cases recorded ectopia lentis was presented in a large proportion of cases (10 out of 18). Terrien cited cases supporting both opinions—one in which no familial nor hereditary antecedents could be found, and another, the case of a little girl with congenital ectopia of the lens in both eyes, in which the defect appeared in three and probably in four generations. Burch, Lloyd, Haas, and Weve believe that the condition shows a hereditary or familial tendency.

The mechanism determining arachnodactyly and its anomalies remains obscure. Terrien advanced two principal theories: the first, described by Weve, the Dutch observer, favors a congenital mesodermic dystrophy; the second, that the disease is hypophyseal in origin.

1. Congenital mesodermic dystrophy is an embryonal alteration, a form of elective dysplasia of the tissues originating in the mesoderm. This theory, however, does not explain the decalcification of bone, nor the changes in the lens and the zonule that originate in the ectoderm. During intrauterine life a dystrophic change of perilenticular vascular tissue may occur, and this vascular tissue does have its origin in the mesoderm. Any alteration in lens nutrition would explain smallness of the lens. The lens would then not be able to keep up with the zonule which follows the growth of the eyeball, its fibers would be stretched and then broken, as was observed by Terrien in lens displacement.

2. As to the theory of hypophyseal origin of the syndrome, from the researches of Pierre Marie, gigantism or acromegaly is due to a lesion in the hypophysis, in the anterior lobe of the gland, characterized by multiplication of eosino-

phile cellules which secrete the growth-hormone (the somotrope). In the adult this hyperactivity determines acromegaly; in the child or adolescent it constitutes gigantism; in the fetus it engenders dolichostenomelia (arachnodactyly). However, Marfan declared that biologic experiments have not given decisive results, and that defective functioning of the hypophysis is too inconsistent and insignificant to acount for all the disturbances that make up the syndrome.

The mixed theory of François (Soc. franç. d'Opht., 1935) held that the condition is due to hypersecretion of the hypophyseal hormone of growth, in addition to a dystrophic hypersecretion of the anterior lobe of the pituitary gland, which stimulates growth of bone and muscle.

Marfan objected to the mixed theory, asserting that there is no relation between his syndrome and alterations in the cord. Terrien suggested that the displacement of the lens, along with the skeletal changes, may be due to the growth hormone's exciting too rapid a development of the scleral envelope of the eyeball, a development with which the zonule could not keep up and thus not prevent the lens displacement.

In his recent paper (1938) Marfan discussed four theories of origin of the syndrome; namely, that it is: (1) of germinal origin; (2) of mesodermal origin; (3) of hypophyseal origin; (4) due to "status dysraphicus." Marfan treated this last in detail, but believed that it does not explain the malformations of the syndrome. All these theories can be challenged by critics.

Marfan offered no hypothesis of his own, but drew attention to the large part the hypophysis plays in the pathogenesis presented by all the others.

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GLAUCOMA ASSOCIATED WITH HYALINE BODIES (DRUSEN) OF THE OPTIC DISC

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Drusen or hyalinelike bodies of the optic nerve head are quite rare. They were first described in 1858 by Heinrich Müller[1] who found them in both eyes of a 75-year-old man who had been blind. Müller stated that they resembled the "drusen" bodies found in the lamina vitrea. Liebreich,[2] in 1868, was the first to observe the condition ophthalmoscopically. Ninety-six cases have been studied clinically, and a number of these have later had histological studies, in all 28 cases.

Drusen bodies appear as whitish, grayish, or yellowish, translucent, refractile masses, either discrete or in clumps on the optic disc. They often overlap the disc margins or they may occupy a position deep in the sclerochoroidal canal. When they cover the entire disc they present a single nodular mass, and the form may be that of a mulberry. They may project for several diopters into the vitreous. The swollen appearance of the disc has often suggested optic neuritis, but inflammatory reaction is absent. Drusen bodies usually occur in both eyes and are found in both the old and the young, but most of the cases reported have been in adults beyond middle life. The age of the youngest patient reported was eight years. Generally these bodies produce no symptoms. In about one third of the recorded cases there was reduced vision. Scotomata and contracted form and color fields have frequently been reported. Such visual and field changes are thought to result from pressure atrophy of the nerve fibers when the masses are situated in the sclerochoroidal canal.

While the exact nature of the bodies is not known it is now generally believed that they are composed of hyaline or a hyalinelike substance. Tobler[3] was unable to dissolve them in water, alcohol, ether, acetic acid, or potassium or sodium hydroxide. Calcium deposits have frequently been found in the drusen bodies studied microscopically.

The origin of hyaline bodies is not firmly established. Müller considered them to be outgrowths of the lamina vitrea. Parsons[4] believed that, in some cases at least, they originate from inflammatory exudates in the disc. Fuchs[5] held that they are derived from neuroglia cells in the disc. Collins and Mayou[6] are of the same opinion and base it on the fact that neuroglia cells have origin similar to the pigmented cells of the retina which commonly produce drusen of this structure, and also on the fact that these bodies are formed frequently in eyes afflicted with retinitis pigmentosa, in which disease there is an overgrowth of neuroglia. A slightly different theory is advocated by Lauber[7] and others who contend that drusen develop from misplaced pigment epithelial cells in the disc. This view is given support by the occasional finding of pigment deposits in the papilla. Michail[8] recently described four such incidents.

A few cases have been followed over a considerable period of time and most have shown little or no change in the ophthalmoscopic appearance. Gifford[9] thought, however, that the mass in his first case had enlarged somewhat after two years. Lauber noted an increase in elevation of from 1.5 to 3 D. in three patients, a mother and two daughters, over a period of several years.

Heredity undoubtedly is an important factor in the etiology. Ancke[10] reported two families in each of which three out of

five children had retinitis pigmentosa and five of these six showed drusen bodies of the disc. Braun[11] observed the condition in two generations of two different families. Leimgruber[12] found, in 41 members of five families, 23 individuals afflicted with drusen. He considered this to point strongly to a dominant mode of inheritance of the condition. Altogether this author collected 10 families with two or more members showing hyaline bodies of the disc. Hereditary syphilis was thought to be a factor in the etiology by Bernacka-Biesiekierska and Wieczorek.[13] These authors observed two boys and a girl in a family of seven children with peripapillary hyaline bodies. There was congenital syphilis in the family, and the hyaline bodies were found only in those children exhibiting ocular characteristics of this disease. There is little further evidence, however, to indicate any etiologic relationship to syphilis.

In a large percentage of the cases of drusen reported there have coexisted other ocular conditions. The relationship in most of these is doubtless accidental. It is significant, however, that the condition in at least 13 individuals has been associated with retinitis pigmentosa (Nieden,[14] Oeller,[15] Masselon,[16] Ancke, Remak,[17] Stanford Morton and Parsons,[18] Tillé and Trantas,[19] McKenzie,[20] Goldstein and Givner[21]). Story[22] reported the condition in an eye with anomalous distribution of the retinal arteries. In one of Stood's[23] cases there was anastomosis of two arteries in one eye and a persistent hyaloid artery in the other. Rabitsch[24] reported a case with congenital opacity of the lens. Posterior cortical cataract was present in the case described by Tillé and Trantas. DeSchweinitz's[25] patient, presenting the first case to be reported in America, had been shot in the head 20 years before. Two of Nieden's[26] cases followed severe head injury. Gessner[27] found drusen in a case of traumatic enophthalmitis.

Lawson[28] and Löhlein[29] reported cases associated with chorioretinitis. The former's case was thought to be syphilitic and the latter's inactive tuberculosis. Gifford described the case of an 11-year-old girl with thrombosis and occlusion of several branches of the retinal artery. The mass completely occluded the disc and extended onto the retina, in one direction, as much as 2½ disc diameters. It was elevated nine diopters. Vision was reduced to doubtful light projection. The other eye was normal. Drusen were associated with pseudoneuritis in a case reported by Bonhoff.[30] Fejer's[31] patient had brain tumor. The drusen were bilateral and one eye was blind. Among other neurological conditions there was bilateral third-nerve paralysis. The patient in one of Lauber's cases had pituitary tumor. Another had tobacco-alcohol amblyopia with a central-field scotoma. Neuroretinitis accompanied drusen in a case described by Noyes (mentioned in discussion of deSchweinitz's case). The patient had scarlet fever and albuminuria at the time examined.

Atrophy of the optic nerve, in most cases thought to be due to pressure from the drusen bodies, was recorded by a number of authors (Müller, Lauber, Remak, Stood, Streiff,[32] Thompson[33]). Streiff, in 1904, recorded five cases, one of which showed atrophy and two of which developed drusen following choked discs. In one the drusen were noted three years after and in the other ten months after observation of the choked discs. DeSchweinitz's patient had atrophy but not as the result of the drusen.

Contracted fields, in cases other than those associated with retinitis pigmentosa, were found a number of times (Stood, Nieden, deSchweinitz, Streiff, Rabitsch, Lauber, Fejer, Lordan,[34] Hoeg,[35] Juler[36]). In Gifford's second case, there were contracted color fields. Juler's case with field

contraction also showed a central scotoma. In a case reported by Rabitsch and in four of Lauber's there were small paracentral scotomata but no enlargement of the physiological blind spots. Nieden's patient, a man 29 years old, presented a contracted field for blue. Nieden believed this due to pressure of the hyaline bodies on the nerve fibers. There was no arterial pulse, nor could this be elicited by pressure on the globe.

In 1904 Demaria[37] studied the eye of a patient removed following an operation for glaucoma and found a mass of "amyloid bodies" filling the sclerochoroidal canal. There were complete atrophy and a deep glaucomatous cup. Demaria felt that the "amyloid bodies" had developed after atrophy had taken place.

In discussing drusen of the papilla Fuchs makes the following statement, ". . . much more frequently are they found in preparations of diseased papillae and particularly do they occur in glaucomatous or atrophic changes of the optic nerve." This appears to be the only direct reference in the literature to any relation to glaucoma, and Demaria's case the only recorded instance of the two conditions existing in the same eye.

Case report

A 19-year-old hotel waitress consulted me on May 15, 1936, because of sudden loss of vision in the left eye. Two days prior, while at her work, she suddenly became a little dizzy, felt like fainting, and "seemed to be in a fog." Shortly thereafter, she noticed that she was unable to read with the left eye. There was no pain in the eye but a slight, dull ache above the brow. The vision gradually became more foggy.

Her general health had always been good. Two weeks before she had had a rather severe head "cold." Her menstruation was rather excessive and there was generally some backache at that time. She had had no previous eye trouble.

The right eye appeared to be normal externally. The bulbar conjunctiva of the left eye was slightly injected and the eye appeared to be slightly proptosed. The cornea was a little hazy, and there were two or three small spots arranged in a vertical line on Descemet's membrane below the pupillary center. The pupil was somewhat larger than that of the right eye, measuring 4½ mm., but reacted fairly well to light and convergence. The anterior chamber was of normal depth, and the angle was in no way obstructed. The iris showed no engorgement nor thickening. The eye was hard to the touch. With the Gradle-Schiötz tonometer the tension was 52 mm. Hg. The tension in the right eye was 14 mm. Aside from the cornea of the left eye, the media were clear throughout.

The optic disc of the left eye presented a striking appearance. It was described at the time as resembling a clump of yellowish fat globules. The outline was very irregular due to five or six large, and four or five smaller, yellowish, translucent, rounded bodies which nearly obscured the upper half and a portion of the lower margin of the papilla and overlapped the retina. The largest of these were about one third the diameter of the papilla. The vessels passed over or between the nodules. The highest point of elevation was one diopter above the retina. The small portion of the disc visible was of normal color, and there was no abnormal cupping. On the disc, the retinal artery showed a bounding pulsation. The veins were not notably engorged, and no other abnormalities were found. The papilla of the right eye presented 18 or 20 similar but much smaller nodules, which did not distort its shape. There was no pulsation.

Vision in the right eye was 20/15—, and in the left eye 20/30, but very foggy.

The visual fields were normal in outline in each eye. Ocular rotations were normal. There was an exophoria of 1½ D. for distance and 20 D. for near. A diagnosis of drusen of the optic discs with non-inflammatory glaucoma of the left eye was made, and the patient sent to the hospital, where 1-percent pilocarpine nitrate was instilled once every hour. The blood Wassermann reaction was negative. The general physical examination was entirely negative. There was no elevation of temperature. The patient was in robust health.

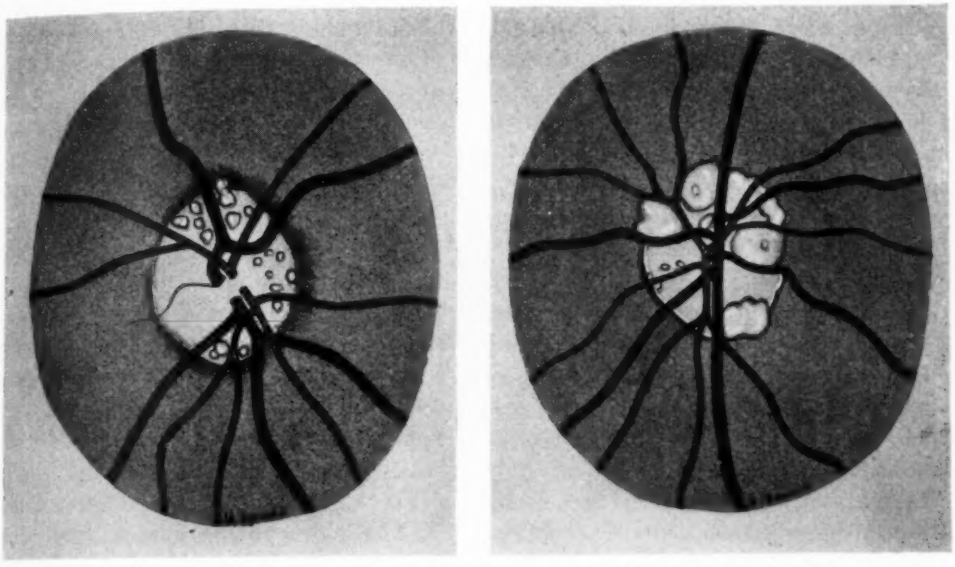

Fig. 1 (Athens). From left to right—drusen of the papilla of the right eye and of the left eye.

On the following day the cornea had cleared, the pupil was quite small, and the intraocular tension was 35 mm. Hg. The vision was no longer foggy. Four days later the tension was 18 mm. compared to 14 mm. in the right eye, and the vision was 20/15. X-ray studies revealed no evidence of intraorbital or intracranial pathology. The patient left the hospital on May 20th, but was seen frequently for several days, and pilocarpine was continued but less often. On May 27th pilocarpine was discontinued. The tension was checked about once a week until July 3d and remained equal to or below that of the right eye. More careful and detailed fields were taken on June 10th. The form fields were normal in outline. The physiological blind spots were uniformly enlarged, that of the right eye was thought to be out of proportion to the amount of drusen. No other scotomata were found. The color fields were in their normal relation but the fields for blue were slightly contracted in the upper temporal quadrants in both eyes. The refraction was essentially normal.

The patient had no further symptoms of glaucoma until Sept. 2d, when she again noted blurring of the vision. She was seen on the following day, when the tension was found to be 42 mm. Hg in the left and 14 mm. in the right eye. Pilocarpine was resumed, an instillation every four hours. She lived some distance away and did not return until September 8th, when the tonometer showed a tension of 17 mm. in the right and 25 mm. in the left eye.

The next attack came on March 3, 1937, with blurring of the vision. The

patient used pilocarpine at home and the vision cleared somewhat. However, on the following day the tension was found to be 38 mm. Hg. On March 10th the tension was down to 18 mm., equal to that of the right eye. Another attack occurred on September 12, 1937. The patient was seen on September 14th, with tension of 32 mm. in the left eye and 14 mm. in the right. The tension was again promptly brought under control. At my request the patient returned on May 24, 1938, for drawings of the fundus. She stated that she had had two attacks since last seen, when the vision was slightly blurred. These came on toward evening, and she had used pilocarpine. The next day her eye seemed to be quite normal. On this visit the vision and tension were normal.

Two years later, March 7, 1940, she came for refraction, stating that occasionally when very tired or nervous and at the time of her menstruation the vision in the left eye would slightly blur. A good night's rest usually cleared it up. She had learned to estimate her own intraocular tension and watched this carefully. She felt that it had not been appreciably elevated for over two years. Epinephrine hydrochloride 1:1000 in the conjunctival sac did not dilate the pupil. There was some headache and discomfort on close use of the eyes, which, it was felt, was definitely due to convergence insufficiency. Visual fields were again charted. There was no appreciable change in the form fields, blind spots, nor in the color fields of the right eye. The left eye, however, showed marked contraction for blue, which was within 5 degrees of the fixation center and inside the fields for red and green. The red was slightly reduced.

The patient was last seen July 25, 1940. She had no complaint but came because she happened to be in the city. She stated that two weeks previously she had had an attack of blurred vision. For some reason she did not use her drops and the vision cleared up after four days. The tension was 12 mm. in the right eye and 17 mm. in the left. There was no change in the fields. Vision remained at 20/15.

Throughout this period of observation of over four years there was no alteration in the ophthalmoscopic appearance of the fundi in either eye. The only change consisted in contraction of the color fields, notably the blue, in the glaucomatous eye.

During this period opportunity was afforded for examining the eyes of the father, mother, and three younger sisters. Aside from low-grade refractive errors, they were entirely normal. There was also a brother who was never examined but who was thought to have normal eyes. Neither the patient nor her parents could recall any relative with defective vision.

On the relationship of glaucoma to the hyaline bodies in this case, one can only speculate. Aside from the age of the patient, quite young for glaucoma, and from the fact that glaucoma occurred in the eye with the most extensive involvement with drusen, there is nothing to suggest more than a coincidence. Mechanical compression of the retinal vein at the disc without hemorrhage or exudate would seem hardly sufficient to produce such a rise in intraocular tension.

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TUMORS OF THE OPTIC NERVE

Study of thirteen cases from Brazil. Diagnosis. Degree of malignancy. Clinical classification. Histopathologic classification. Relation to von Recklinghausen's disease. Methods of surgical treatment

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Primary tumors of the optic nerve are extremely rare. De Wecker stated that many ophthalmologists, even those of long experience, often went through their lives without encountering a single case. In the most recent monograph on this subject, the extensive and monumental work of Davis (Arch. of Ophth., 1940, April and May), this rarity is well demonstrated. Among other citations, this author says that Verhoeff found four cases of primary tumor of the optic nerve during a period of 36 years among 669,557 patients examined in the Massachusetts Eye and Ear Infirmary. Today the total number of cases observed and published in the world's literature certainly reaches 400. It is probable, however, that this rarity is not a true expression of the incidence; many cases may be missed in examinations that are not made systematically and thoroughly.

In Brazil, I know of 13 cases. I do not know to how many patients this number corresponds, but I can say that five of these cases from my practice (private and hospital) were found among slightly over 100,000 patients examined. I report herewith the cases from Brazil:

Case 1 (1912, Dr. José de Souza Pondé). Primary neuroglioma of the optic nerve. Enucleation of the globe and extirpation of the tumor. Period of observation: two years.

The case of Souza Pondé was observed in May, 1912. The patient was a female, four years of age, from his private practice. The child was healthy and well developed, with brown eyes and black hair. According to the information gathered from her mother, the baby was born at term. At the age of three years she had a severe febrile illness accompanied by severe headaches, somnolence, and convulsions, from which she recovered completely; six months afterwards her parents began to notice that the left eye of the child was becoming more prominent than the right and brought her in for examination. The parents were healthy, with 13 children all in good health. The patient's aunts and uncles were likewise in good health.

Ocular examination: The *left eye* was much more prominent and open than the right eye. The forward exophthalmos could not be measured. The eye could be moved in all directions. Palpation revealed nothing except irreducible exophthalmos. There was no pain. The ocular media were transparent. The pupil was more dilated than that of the right eye and not reactive to light. Skiascopy revealed astigmatism and hypermetropia of three diopters. The papilla was pale, with poorly defined margins, and projecting, narrowed vessels; the whole indicative of a previous papilledema. Vision was nil. The *right eye* was entirely normal with vision equal to 1.00.

The diagnosis of primary tumor of the optic nerve was made. It was decided to enucleate the globe, followed by extirpation of the tumor. The tumor was ovoid in shape and of hard consistency. It weighed 15 grams and occupied the whole length of the nerve. It was not adherent to the

other tissues of the orbit. One year and nine months after operation there had been no recurrence of the growth.

The microscopic examination was made by Dr. Leoncio Pinto who diagnosed the tumor as a "primary neuroglioma of the optic nerve." The following is taken from his description: "The tumor was fixed in Bouin's fluid. Section showed the presence of a grayish tissue with definite points of degeneration, especially in the central portion, which revealed a yellowish mass indicative of cellular separation and disintegration. In the periphery the tissue was normal. The sections were stained with Masson's hematoxylin-eosin-saffran stain, and showed tissue of slender fibrillae in a network of red staining with open-walled vessels, zones of hemorrhage, and pseudo-cysts. The parenchyma consisted of rounded cells with poorly developed cytoplasm containing deep-staining nuclei. The fibrillar appearance with the disposition of its fibers and with its rose color showed the structure of a neuroglioma. The exact pathologic diagnosis was confirmed by stains by the method of Mallory, which showed the characteristic red color of neuroglia and by the method of Mallory-Ribert in which the stain was negative. This excluded any other kind of tumor. The cellular structure, poor in cytoplasm and rich in nuclei, was another confirmation of neuroglioma of the optic nerve."

Case 2 (1918, Dr. Pereira Gomes). Incomplete observation of a primary tumor of the optic nerve. This patient was not seen again after the diagnosis was made. Operation was refused (fig. 1).

A boy, six years of age, was brought to my office on August 7, 1918. The parents and three siblings were in good health. The laboratory examinations were negative. The right eye was prominent, exophthalmic, and deviated downward and outward, with moderate restriction of the movements of elevation and inward rotation. The ocular media were normal. There was postpapilledema atrophy of the papilla. Vision was nil. The left eye was normal and had normal vision. Upon advice to hospitalize the child for complete studies and operation, the father refused to give his permission and the patient was not seen again.

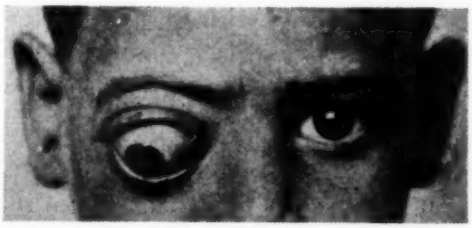


Fig. 1 (Pereira Gomes). Six-year-old boy in case 2.

Case 3 (1919, Dr. Pereira Gomes). Primary intradural tumor of the optic nerve. Enucleation followed by extirpation of the tumor. No recurrence. Period of observation: 21 years.

F. O., a seven-year-old healthy female, a native of São João da Bocaina, was brought to my office on November 20, 1919. Attention had been called to her right eye, which was exophthalmic, strabismic, and prominently visible between her widely opened lids. Six brothers and sisters were well, two others, twins, having died of gastro-enteritis. Her aunt told me that the patient's grandparents, aunts, and uncles were healthy, and that the little one had had measles and grippe, but had never received any injury which might have caused her trouble. "This child," said her aunt, "has been ill for 15 to 18 months, but has never complained of pain in the affected eye, which has never been inflamed." The first sign of disease that her parents noted was a convergent strabismus that developed gradually and was followed by increasing prominence of the eyeball. The child never complained of

reduction of vision nor of diplopia. The parents were first made aware of the defective vision of their child after consulting a physician in Jahu. Several months later they came to São Paulo, where the patient was seen by two specialists. The first one advised mercurial inunctions. The second, under whose observation the patient remained for almost a year, recommended a continuation of the same inunctions and gave a series of neosalvarsan injections." Complete examination of the pearance, and the periphery was normal in color.

There was an exophthalmos of 12 mm., not reduced by pressure, and without pulsation. A paralytic convergent strabismus was present, with the eye turned down and in. The position of the eye was due to paralysis of the sixth nerve, the fourth nerve, and a partial paralysis of the third nerve, affecting the superior-rectus and inferior-oblique muscles, permitting the eye some movements downward and in-

Fig. 2 (Pereira Gomes). Seven-year-old girl in case 3. Paralytic convergent strabismus.
Fig. 3 (Pereira Gomes). Same patient as in figure 2, following operation.

urine proved it to be normal. Complete clinical examination showed no other pathology. Wassermann reaction was negative. Nose and throat examination, including the sinuses, was negative. Roentgenograms were negative for the presence of tumor and for involvement of the periorbital bones in the excellent plates furnished by Dr. Raphael de Barros.

Ocular examination. Right eye: The palpebral fissure was widely opened, especially in its outer two thirds. The lids, conjunctiva, cornea, anterior chamber, and iris were normal. The pupil was round and more dilated than that of the other eye; it was immobile, both to direct and consensual light reaction. The lens and vitreous were normal. The fundus showed postneuritic optic atrophy. The papilla was poorly demarcated, recognizable only by the position of the vessels, consisting of filiform arteries and tortuous engorged veins. There was an absence of pigmentary foci or hemorrhages. The retina around the disc had a pearly ap-

ward (fig. 2). Skiascopy under mydriasis showed eight diopters of hypermetropia. The keratometer showed a slight astigmatism against the rule. Vision was nil. Deep palpation of the orbit, facilitated by the exophthalmos and by the docility of the patient, revealed no sensation of a tumor nor of adhesions of the tissues. The globe could be moved with ease to all sides of the fingers of the examiner.

The *left eye* showed no abnormality except a hypermetropia of four diopters. Vision was normal with a convex lens of three diopters.

With these clinical findings, together with a knowledge of the differential diagnostic elements, the diagnosis of tumor of the optic nerve was made. It was decided to operate by removing the globe, followed by extirpation of the tumor.

Operation: This was performed on December 2, 1919, with the assistance of Dr. Paulo de Aguiar. The globe was enucleated, following which was removed an enormous intradural tumor of the optic

nerve which extended up to the optic foramen. A double piece of the removed tissue was immediately turned over to Prof. Dr. Walter Haberfeld, who furnished us with the following description:

Macroscopic examination: The complete eyeball was slightly flattened anteroposteriorly, measuring 2.1 cm. in its longitudinal diameter and 1.9 by 2.3 cm. in the transverse diameters. The anterior segment of eyeball was normal; the pupil regular and dilated. The tumor was separated from the globe at the entrance of the nerve. The nerve was 2 mm. in diameter there and ashy in color. The retrobulbar tumor weighed 5.5 grams, and measured 3.2 by 2.1 cm. in size. It was oval in shape and was enveloped by a thin membrane, bluish white, with small oval hemorrhagic zones arranged transversally. On cutting the tumor there was seen in its middle a band, measuring 5 mm. to 6 mm. in diameter, which ran through it more or less in its center axis. It was of ashy color, gelatinous, ending posteriorly by a rounded button. This band, the original optic nerve, was not separable from the tumor mass, which was completely fixed to the sheaths of the nerve and probably to the nerve itself. The tumor was ashen in color and gelatinous in appearance in the portion closest to the nerve; the remaining part, also gelatinous, was an intense red color and less firm (figs. 4 and 5).

Histopathologic examination: Longitudinal sections were made at different levels across the optic nerve and tumor. Stains used were hematoxylin-eosin, Van Gieson, Marchi, and Weigert-Pal. A description of the section follows: The tumor consisted of a large number of very small cells with nuclei of the same size or generally smaller than those of lymphocytes. The protoplasm was scant and poorly defined. In addition to these small nuclei, rounded, rich in chromatin, and without chromatic structure, others existed of double the size, or even larger, with a fine chromatic structure. In other places the cellular structure was larger, somewhat like plasma cells, the cells of little protoplasm being disposed about the poles of the oval nuclei and ending in the form of a fine point which became lost in a protoplasmic reticulum in which it was located. This reticulum consisted in a coalescence of large protoplasmic masses with a gross or fine trabecular distribution yet always with a sharp limit. With the stain of Van Gieson this reticulum was clearly yellow (fig. 6). In addition to these cells were others, located in the neighborhood of the capillaries and precapillaries, which resembled new fibroblasts; nevertheless, there was no visible production

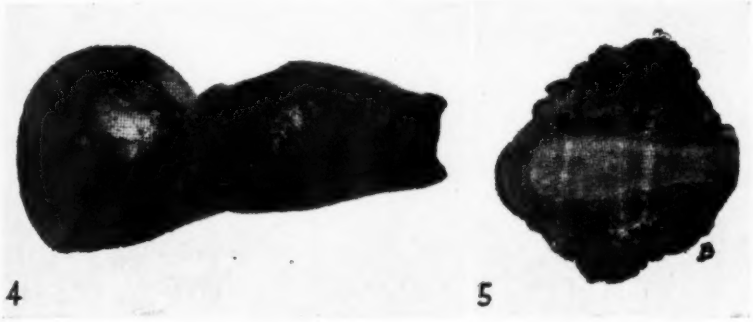


Fig. 4 (Pereira Gomes). The tumor removed in case 3.
Fig. 5 (Pereira Gomes). Sectioned tumor, showing original optic nerve

of connective fibers, which were scarcely encountered in the neighborhood of the vessels. The number of vessels increased in the direction of the optic nerve, as did also the number of connecting fibers the more one approached the old sheaths of the optic nerve, whose connective tissue lost itself in the tumor. In a small extension, more or less in its center, the tumor entered into contact with the optic nerve. It is clearly seen how the sheaths separated the tumor from the nerve tissue; and the farther from the extremity of the section, the more delicate became the connective tissue and, therefore, the less clear the limit between the nerve and the tumor up to the latter's complete disappearance in the place already mentioned. These relations were apparent in the sections stained with Van Gieson's stain. The optic nerve had its connective septa well defined and its nerve fibers were much more rich in cells than normal. One third of this was like the tumor (evidently nuclei of glial cells); the other two thirds were of cells with more vesicular nuclei, poor in chromatin, of elongated oval form, sometimes with irregular margins, in size and appearance like new fibroblasts, but containing nuclei which were two, three, and four times larger. At times these were in apparent amitosis (two, three, four nuclei). Very likely this was due to cells of connecting origin (neuroblasts?), a hypothesis made all the more probable by encountering these cells among the connecting septa.

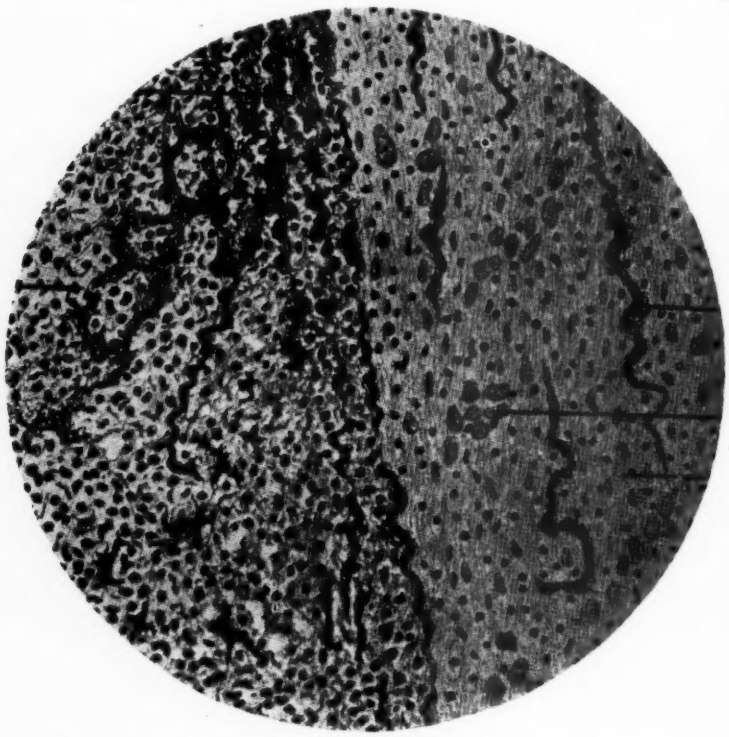


Fig. 6 (Pereira Gomes). Photomicrograph of tumor removed in case 3.

Discussion: This tumor appeared to be a soft malignant glioma of the sheaths of the optic nerve, with beginning invasion

of the latter, which was completely atrophied. This patient is alive today; she is married, has three children, and has never had any more trouble from this eye, for which she has worn a prothesis. She has survived up to now, moreover, almost 21 years.

Case 4 (1920, Dr. W. E. Maffei). Primary tumor of the optic nerve. Personal communication.

Specimens from this unpublished case are in the Archives of the Laboratory of Pathological Anatomy of the Faculty of Medicine of the University of São Paulo, among 13,000 autopsies there performed. J. Q. A., 19 years old, male, a Brazilian (no. 372, February 2, 1920), died of dysentery.

Diagnosis: Solid glioma of the optic nerve, entirely orbital.

Case 5 (1921, Dr. Waldemar Belfort Mattos). Primary intradural tumor of the optic nerve. Operation of Lagrange with preservation of the globe. No recurrence. Period of observation: 8 years (fig. 7).

A white woman, Spanish, a domestic aged 39 years, came from São Paulo. She entered the hospital of Prof. Dr. J. Britto of the Santa Casa de São Paulo on September 27, 1921. She had been married twice, her first husband having died of carcinoma of the stomach. She had had three children by her first husband, one of whom died of pneumonia. By her present husband she had had one son. Her husband and her children were in good health. She had never had an abortion. She had had measles, chickenpox, and diphtheria in her childhood. At the age of 14 years she had had typhoid fever and finally, three years ago, she had grippe. There was no venereal nor syphilitic history. She began to suffer from her present illness six years ago, first noticing reduced vision in the left eye and at the same time a slowly progressive exophthalmos. There had never been pain, nor was there any evidence of trauma.

Ocular examination. Right eye: Nothing abnormal was found except a slight astigmatism against the rule; normal vision. *Left eye:* The palpebral fissure was widely opened; there was hyperemia of the palpebral and bulbar conjunctiva. The lacrimal apparatus was normal. The eyeball was 8 mm. exophthalmic; the exophthalmos was not reducible and not pulsating. The eyeball was deviated out and down. There was normal extrinsic musculature. The cornea, anterior chamber, and iris were normal. The pupil was round, larger than that of the right eye, without direct light reflex, but reacting slightly to the consensual light reflex as well as to convergence and to accommodation. The lens and vitreous were normal. The ocular fundus showed atrophy of the temporal half of the papilla. The borders were well defined, and the pigment ring was normal. The nasal half was reddish with indefinite margins and with a large number of new-formed vessels. There were three vascular loops with convexity directed peripherally, at the side of which were small hemorrhages. The retinal vessels were normal. Vision was nil. Skiascopy: 14 diopters. Slight astigmatism against the rule. Palpation within the orbital rims gave no sensation of a tumor. The globe was freely movable in all directions; the intraocular pressure, normal. Clinical-neurological study by

Fig. 7 (Pereira Gomes). Patient (adult, female) in case 5.

Professor Almeida Prado showed: increased tendon reflexes; resounding second heart sound; Wassermann reaction of the blood positive; urine normal; tuberculin test negative; examination of the nose and sinuses negative, including X rays. With these facts the diagnosis of tumor of the optic nerve was made and anti-

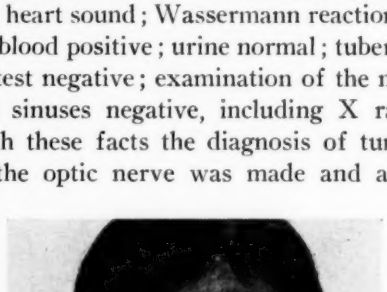


Fig. 8 (Pereira Gomes). Patient (adult, female) in case 6.

syphilitic treatment given for two months without result. Syphilitic gumma of the optic nerve is extremely rare, only one case being found in the literature (that of Verhoeff).

Operation: Operation was performed on December 27, 1921, under chloroform anesthesia, by Dr. W. Belfort Mattos, assisted by Drs. Souza Martins, Valentim Del Nero, and Paulo de Aquiar. The technique of Lagrange was employed—removal of the tumor with preservation of the eyeball. The final result was considered good, although the eyeball remained fixed somewhat, deviating outwardly in a position of slight divergent strabismus. The nutrition of the eyeball remained good, although the cornea lost its sensitivity. The fundus of the eye showed changes: first, the appearance of a large number of white areas similar to those of leukemic retinopathy, and, finally, total atrophy of the papilla with the disappearance of the vascular loops described.

Histopathologic description by Professor Klotz of the Faculty of Medicine and Surgery of São Paulo: The specimen consisted of an oval mass which measured 4 by 2 by 1.5 cm., presenting two cut extremities which represented parts of the optic nerve. In one of the extremities of this specimen, there was a bud separated by a slight constriction from the main mass. The optic nerve at both ends measured 0.5 cm. in diameter. The entire structure, except the extremities, was clothed by a membrane which was an extension of the dura. This extension was pale and of normal thickness. There were no external adhesions nor any evidence of invasion of the tumor through its walls. The tumor was soft and somewhat elastic. A superficial section showed a uniform structure. The tumor was adherent to the dura. It was soft, elastic, and of an ashy-yellow color. The superficial section was moist. There was little stroma in the tissue and the optic nerve could not be seen. There were few blood vessels without hemorrhages. The tissue consisted of a stroma made up of a network of fibrillae among which were spaces which contained a homogeneous gelatinous substance. The cells of the tissue contained small dark and rounded nuclei, more or less the size of lymphocytes. Around these nuclei there was a small amount of cytoplasm, and from this extended numerous fibrillae which constituted the reticulum of the stroma. The cells were of uniform size and appeared scattered without any order throughout the tissue. There were no mitotic figures nor vestiges of the optic nerve. There was connective tissue in small quantities around the vessels. The entire tissue was made up of glial cells.

Diagnosis: Glioma of the optic nerve.

Dr. W. Belfort Mattos examined this patient eight years after operation, according to his report in his book on ocular surgery, published in 1931. The patient was in good health and with no change in the site of operation.

Case 6 (1921, Dr. Jorge dos Santos Caldeira). Primary intradural tumor of the optic nerve. Operation of Lagrange

with preservation of the eyeball. No recurrence. Period of observation: one year (fig. 8).

This observation was published in the Bulletin of the Society of Medicine and Surgery of São Paulo (1922, April, page 56) and in the thesis of Dr. Jorge dos Santos Caldeira quoted in the bibliography. The patient was a 24-year-old, married, Brazilian farmer's wife, coming from Martinho Prado, State of São Paulo. She entered the hospital of Prof. J. Britto at the Santa Casa de São Paulo on February 18, 1922. The family history revealed that her sister, 12 years of age, was blind, the cause not being known. Her personal history revealed the usual diseases of infancy; she had had three children and three abortions. Of her three children two died, the first of convulsive attacks and the second at the age of eight years of an unknown cause.

The patient's left eye had been injured by a twig of a coffee tree four years before. She noted at this time that this eye, which was red and painful for 15 days, had no vision. Six months after that, she began to notice exophthalmos, which increased up to the point seen when she entered the hospital. She had no pain in this eye except when it was hurt, nor did she suffer from any general disturbance. Clinical-neurological examination of the patient showed no abnormality, according to Prof. Ovidio Pires de Campos. The urine was normal. The nose, pharynx, and sinuses were also normal. The feces showed ova of ancylostoma. The blood Wassermann was positive.

Ophthalmologic examination. Right eye: Normal with slight astigmatism with the rule; normal vision. *Left eye:* The palpebral fissure was widely opened, especially internally. The sclera was much thinned, allowing light to be seen through its internal portion when the pupillary area was illuminated. The lids, conjunctiva, anterior chamber, and iris were normal. The cornea was slightly cloudy in its center. The pupil was round, in size equal to that of the right eye, without reaction to light directly or consensually. The lens and vitreous were normal. On palpation of the orbit, a large soft movable tumor was felt behind the globe. There was an exophthalmos of 13 mm., directed somewhat downward. As for the extrinsic musculature, there was free movement except for a slight restriction of the superior and external recti and of the inferior oblique. The patient was able to cover the globe entirely with her upper eyelid, which came well into contact with the lower lid. The ocular fundus showed postneuritic atrophy of the papilla. Vision was nil.

The diagnosis of tumor of the optic nerve having been made, the patient was operated upon on March 9, 1922, by Drs. J. Britto and Pereira Gomes, assisted by Drs. W. Belfort Mattos and Jorge dos Santos Caldeira. The tumor was removed with preservation of the eyeball by the technique of Lagrange. The result was good, notwithstanding that the patient presented one month after operation an external ophthalmoplegia, scarcely appreciable because the palpebral fissure was more narrowed than that of the good eye.

Histopathologic examination by Professor Glotz revealed that the specimen weighed 11.9 grams, measured 4.2 by 2.5 by 1.6 cm., was of oval form, more or less of the size of a pigeon's egg, and of a light violaceous color. The surface was smooth and glistening, showing itself to be enveloped in a thin capsule, apparently a fibrous tissue, which was interrupted at both poles of the specimen by surfaces which corresponded to the cut portions. Vessels of small caliber, much injected with blood, were observed. Palpation showed it to be of soft consistency without firm nodules within. Nowhere was

there observed the existence of a liquid substance. On sectioning, at first sight near one of the poles of the piece, a cystic cavity was seen, the size of a hazelnut, containing in its interior a soft dark tissue of the size of a pea, attached by a pedicle on one side.

Microscopic examination: Under the little strand of fibrous tissue which enveloped a border of the microscopic section, formed by numerous delicate fibrillae which intercepted each other in all directions, there was an areolar tissue in which were observed glial cells with round nuclei and characteristic star-shaped protoplasm. In some places in relation with these trabeculae and areolae were seen connective fibers, hemorrhagic foci, small areas containing hyalin substance, numerous vessels, some of which showed hyalin degeneration, and remains of the optic nerve made up of bundles of parallel cellular elements which ran through the preparation in a determined direction.

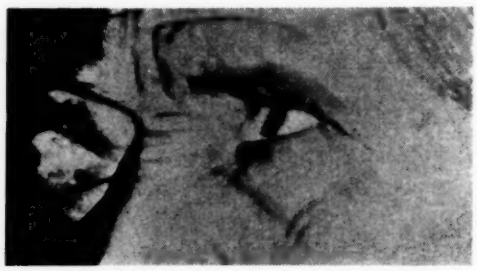


Fig. 9 (Pereira Gomes). Patient (adult, female) in case 7.

Diagnosis: Fibroglioma of the optic nerve with central cystic degeneration.

Case 7 (1929, Dr. Fabio Belfort). Tumor of the optic nerve with extension into the cranial cavity. External orbitotomy of Rollet, with partial exenteration of the orbit. Death 13 days after operation (fig. 9).

R. M. S., a widow, Brazilian, white, 56 years old, registered at the Institute Penido Burnier, of Campinas in October, 1929. Eighteen years before, she began to notice disturbances in her right eye, with pain and reduction in vision, phenomena which lasted for 15 years; exophthalmos began three years later. Examination of the *right eye:* Vision was nil. There was direct irreducible exophthalmos of 34 mm. The extrinsic muscles were intact, but the movements of the eyeball limited. In spite of the exophthalmos the lids could be closed. A retrobulbar tumor was palpable. There was postneuritic atrophy of the papilla. X-ray study of the optic canal showed an increase in the diameter and an increase in the dimensions of the orbital cavity. *Left eye:* Exudates were present in the vitreous; there was peripapillary chorioretinal atrophy, and a partial atrophy of the papilla. Vision was equal to counting fingers at one meter.

Clinical examination: There was a chronic myocarditis. Lumbar puncture showed no increased intracranial pressure; spinal fluid was normal.

Diagnosis: Tumor of the optic nerve.

Operation: On October 21, 1929, an external orbitotomy of Rollet was performed, with removal of the optic-nerve tumor and the eyeball. The patient did well for the first few days after operation, but 13 days after operation she presented a serious picture with intense dyspnea, congestion, severe chills, pulse up to 140, going on to death one hour later in spite of all measures undertaken for relief.

Summary of the anatomo-pathologic study. Macroscopic examination: The eyeball was of normal size, surrounded by the extraocular muscles and bulbar conjunctiva. A large retrobulbar tumor was found, of the size and shape of a hen's egg, measuring 5.5 cm. in length and 3.5 cm. in width. On sectioning it in its major axis there was noted a superficial, pale, wrinkled area, with small folds in all di-

rections. The optic nerve appeared in the vicinity of the papilla, where it could be traced for 4 mm. behind the globe. There was no extension of the tumor through the papilla. The tumor was encapsulated, lacking a covering only at the level of the optic foramen. The capsule was a part of the tumor and was not simply a reaction of the tissues. The tumor had a fibromatous scirrhous consistency. *Microscopic examination* (Dr. Francisco Mignone of the Faculty of Medicine of São Paulo): A minute microscopic examination led to the diagnosis of extradural meningioma (alveolar psammomatous endothelioma) of the orbital portion of the right optic nerve, with extension through the prechiasmal portion on the same side and compression of the prechiasmal portion on the left side.

Autopsy: This proved the existence of a tumor on the right side of the sella turcica, hiding the right optic foramen and adjacent structures and compressing the left optic nerve. On isolating the tumor its only adhesion was to the optic canal, through which it penetrated. The roof of the orbit was perforated in two places. Dr. Fabio Belfort concluded that there had been extension of the tumor by continuity along the sheath of the optic nerve from its intraorbital portion into the cranial cavity.

Case 8 (1936, Dr. J. Santa Cecilia). Tumor of the optic nerve. Krönlein's operation with preservation of the eyeball. No recurrence. Period of observation: one year.

J. R. S., a 22-year-old male, entered the Ophthalmologic Clinic of Santa Casa de Bello Horizonte, Minas Geraes, on April 22, 1936. The visual acuity of his right eye had been reduced for six years and he had had a right exophthalmos for eight months (fig. 10).

Right eye: Vision was nil; there was atrophy of the papilla. The extrinsic musculature was normal. There was a direct exophthalmos of 7 mm. No tumor was palpable.

An oto-rhinolaryngologic examination was normal.

The patient had been operated upon four years before because of a left frontal sinusitis. The neurologic examination was

Fig. 10 (Pereira Gomes). Patient (adult, male) in case 8.

negative, as were also the urine and the blood Wassermann test. X rays of the optic canals showed an increase in size of the right canal.

Diagnosis: Tumor of the optic nerve.

Operation: On June 24, 1936, a Krönlein operation was performed under sodium evipan anesthesia. There was a satisfactory postoperative course. Final result: Ptosis of the upper lid and paralysis of the extrinsic muscles of the right eye.

Pathologic anatomy: An ovoid tumor weighing 6.2 grams, measuring 30 by 17 mm., a neurinoma.

Case 9 (1937, Dr. W. E. Maffei). Primary tumor of the optic nerve. Personal communication. From the Laboratory of Pathologic Anatomy of the Faculty of Medicine of the University of São Paulo.

O. G., a 20-year-old, married, Brazilian female, died on May 8, 1937, from pneumonia.

Diagnosis: Cystic glioma of the optic nerve, entirely intraorbital.

Case 10 (1939, Dr. Pereira Gomes). Primary tumor of the optic nerve. Operation of Lagrange with preservation of the

globe. Neuroparalytic keratitis, with subsequent atrophy of the eyeball, without intervention. Meningioma of the optic nerve. No signs of von Reckinghausen's disease in the patient or his family. There was no recurrence. Period of observation: one year (figs. 11 and 12).

O. R. F., a Brazilian, white boy, six years of age, living in São Paulo, had a negative family history. The father said that he had noticed an increase in the size of his boy's left eye when he was five years old; also a lump of the lower lid of this eye which showed slow healing. At this time the boy was taken to the outpatient clinic of Santa Casa de São Paulo, where nothing abnormal was noted except for the hordeolum mentioned. In June of 1939, he entered my service at Santa Casa de São Paulo where the necessary examinations were made: Clinical and neurologic examinations were negative; a search for blemishes on his body and on the bodies of his parents and siblings, the blood Wassermann, and urine were all negative. Examination of the feces revealed the presence of ascaris lumbricoides.

Ophthalmologic examination. Right eye: Normal, with normal vision and visual field. *Left eye:* The lids were widely opened; there was an exophthalmos of 7 mm., irreducible, without pulsations, with the globe directed slightly towards the superior nasal side. The cornea was normal; the anterior chamber of normal depth. The pupil was more dilated than on the opposite side, immobile, but contractile by consensual reaction. The examination of the fundus of the eye showed transparent media and postneuritic atrophy of the papilla.

X-ray studies were normal, showing no enlargement of the optic canal nor abnormality of the sella turcica.

A diagnosis of primary tumor of the optic nerve was made and an operation was performed on July 26, 1939, employing the technique of Lagrange with preservation of the eyeball. This technique was altered by a median tarsorrhaphy after removal of the tumor. The postoperative course was normal. Twenty days later, the tarsorrhaphy was freed. Incidentally, several days later, there developed a neuroparalytic keratitis in the eye that had been operated on, which went on to atrophy in spite of all attempts to save it. This, however, offered a suitable bed for a prothesis. It is interesting to compare the two photographs taken three months apart (figs. 11 and 12); they demonstrated clearly the favorable effect of the operation upon the appearance of the patient.

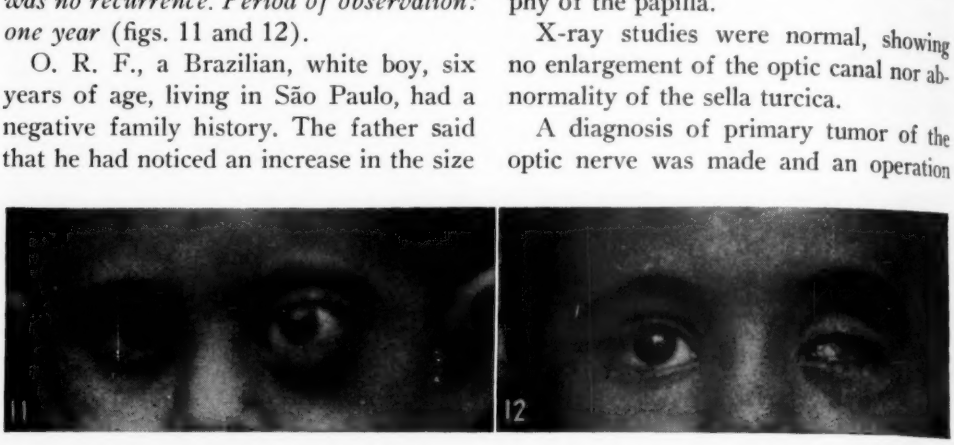


Fig. 11 (Pereira Gomes). Patient, six-year-old boy, in case 10.
Fig. 12 (Pereira Gomes). Same patient as in figure 11, three months later.

The tumor was sent to the Faculty of Medicine of the University of São Paulo. Prof. Dr. Carmo Lordy, who made the histopathologic examination at my request, sent me the following description:

Histopathologic examination: From a study of different sections through the dis-

tal part of the optic nerve, stained by different methods, it was possible to draw the following conclusions. The infra-arachnoid space in almost half the circumference of the nerve was distended and deformed by the retention of spinal fluid. Corresponding to this, in the pia mater and in the respective peripheral part of the nerve, were noted sections of numerous new-formed capillaries of small and medium caliber, some lined by endothelium which was thicker than normal, containing a lipoid substance. In the remaining part of the section the nerve presented more pronounced alterations in its structure with small foci of necrosis, besides other hemorrhages. One was dealing, it seemed, with a simple meningo-hemangioma of the optic nerve (figs. 13 and 14).

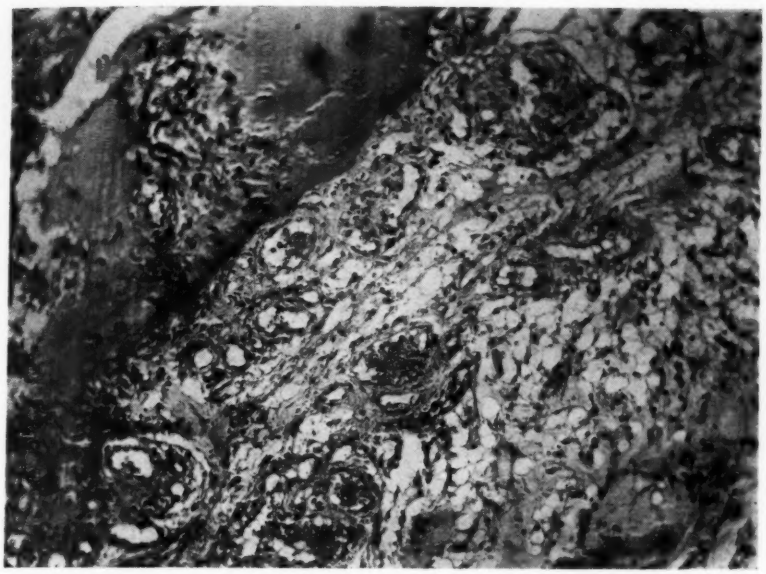


Fig. 13 (Pereira Gomes). Transverse section of the optic nerve in which is noted, at the left and above, an enlargement of the infra-arachnoid space, deformed by the retained spinal fluid, and below numerous cross sections of new-formed capillaries. At the right in the lower corner is a small focus of necrosis. (Hematoxylin and eosin stain, Leitz obj. 3 and oc. 8.)

Case 11 (1939, Drs. Pereira Gomes and Carlos Gama). Tumor of the optic nerve with intracranial extension. Double surgical intervention: Transfrontal craniotomy and partial exenteration of the orbit (enucleation of the globe and extirpation of the tumor). No recurrence. Period of observation: one year.

F. G., a 14-year-old male, white Brazilian worker from Silvianopolis, State of Minas Geraes (fig. 15), entered the service of Dr. Pereira Gomes, in the Santa Casa of São Paulo, on October 18, 1839. The family history was of no significance. The patient smoked 20 cigars a day. No history of trauma. The patient stated that he had had severe frontal headaches for two years followed by pains in his left eye and reduction in the vision of this eye. Then exophthalmos developed and complete loss of vision of the affected eye. For three months, there had been increase in the exophthalmos and headaches, accompanied by nausea and vomiting. On three occasions there had been luxation of the eyeball, twice replaced by his father

and once by his own efforts.

Examination: The clinical examination was normal. The neurologic examination showed pain referable to the trigeminal area, symptoms of increased intracranial pressure, and a facial asymmetry due to the enormous exophthalmos and the increase in size of the orbit. The spinal fluid showed increased pressure, albumino-cytologic dissociation, and positive benzoin reaction in the middle zone.

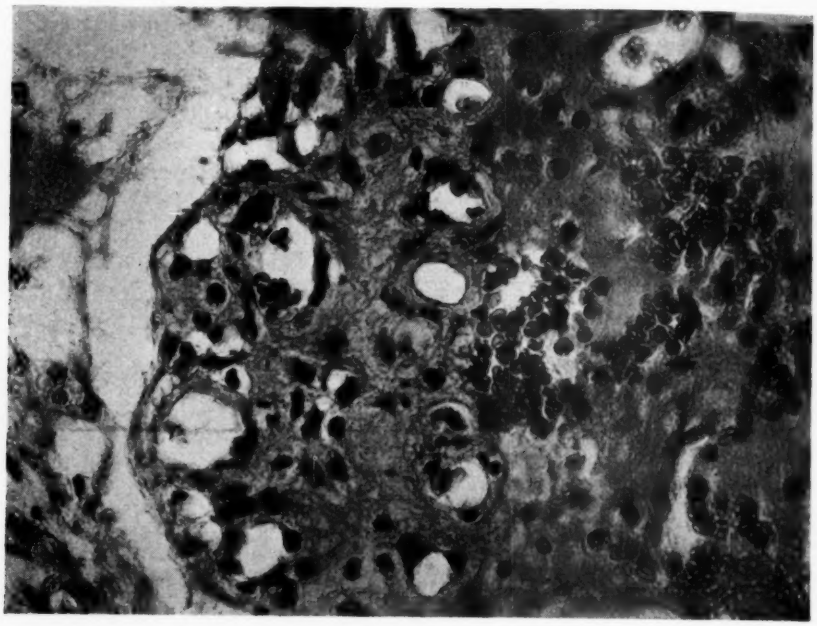


Fig. 14 (Pereira Gomes). An area of the same section as in figure 13 demonstrating in greater enlargement cross section of the new-formed capillaries and a hemorrhagic focus. (Hematoxylin and eosin stain, Leitz 1/12 and oc. 8.)

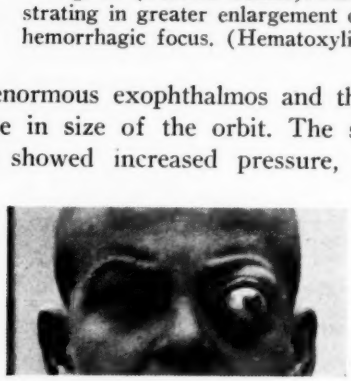


Fig. 15 (Pereira Gomes). Patient (14-year-old male) in case 11.

Cranial X-ray studies showed an increase in the size of the left orbit, left optic canal, and left sphenoidal fissure, and signs of increased intracranial pressure. *Right eye:* There was normal vision and a normal visual field. *Left eye:* An exophthalmos of 15 mm. was directed externally. The lids could not be closed normally, nor could the eyeball be covered, so that the patient constantly pushed down his upper eyelid. The extrinsic muscles functioned normally. The exophthalmos was not reducible nor pulsating; there was no ocular hypertension. A retrobulbar tumor was palpable and movable at the orbital rim. The cornea and media were normal. There was absence of pupillary reflexes. Neuroretinitis was present with edema. The nerve head was recognizable by the convergence of the vessels. Vision was nil.

The basal metabolic rate could not be measured. Ventriculography with lipiodol showed the existence of a large tumor in the infundibulo-chiasmatic-hypophyseal region, obstructing the two foramina of

Munro. Craniotomy, to remove the intracranial portion of the tumor, was first decided upon, with a later orbital operation including a probable enucleation of the globe.

Left fronto-temporal-parietal craniotomy, under local anesthesia, was performed by Dr. Carlos Gama, assisted by Dr. Rolando Tenuto, on October 26, 1939. The procedure was purposely slow (three hours) with employment of the electric bistoury. Four perforations were needed with the electric trephine of DeMartel, joined by the helicoid saw, continuing the bony fracture, a little above the superciliary region. The roof of the orbit was carefully exposed and the tumor seen. It was wine colored, flaccid, globular, encapsulated, apparently adherent to the neighborhood of the left optic foramen. The ophthalmic artery entered the orbit through the sphenoidal fissure by a congenital anomaly. The complete removal of the tumor necessitated sectioning of the left anterior horn of the chiasm, which resulted in a hemianopsia of the right eye. Histopathologic examination of the tumor revealed a cellular glioma of the optic nerve. The postoperative course was uneventful and afebrile, permitting orbital surgical intervention eight days later.

Orbital intervention. (Dr. Pereira Gomes, November 3, 1939, assisted by Dr. Durval Prado) : This procedure, performed under local anesthesia, consisted in the enucleation of the eyeball and the removal of the intraorbital tumor. No other operation could have been undertaken, since the cornea of the exposed eye was ulcerated. The postoperative course was favorable, and the pains disappeared. Figure 16 shows the globe with the tumor of the optic nerve. The basal metabolism test was almost normal (15 percent). Examination of the right eye showed a temporal right hemianopsia. The spinal fluid showed a lowering of the albumin content from 0.40 to 0.10, and a leucocytosis of 180 cells attributable to the bleeding from the intracranial operation. X-ray studies revealed the large craniotomy and the numerous silver clips employed for hemostasis.

The patient was subjected to deep radiotherapy postoperatively. Only one

Fig. 16 (Pereira Gomes). Globe with tumor removed in case 11.

serious complication developed, a hemiplegia with aphasia; this had almost disappeared when the patient was discharged, three months after the last operation. A prothesis gave a satisfactory cosmetic appearance. Histopathologic examination of the tumor in its orbital portion showed it to be identical with its intracranial portion.

Case 12 (1939, Drs. Santa Cecilia and Carlos Gama). Tumor of the optic nerve, with intracranial extension. Death of the patient.

This case deals with a 15-year-old girl from the service of Dr. Santa Cecilia, of Bello Horizonte, State of Minas Geraes. The patient had a unilateral left irreducible exophthalmos of 9 mm., with barely quantitative vision. The papilla was pale and edematous. The left optic foramen

was enlarged (5 mm.). The patient, who reported an injury over two years before, was also examined by Professor Jeandelize, of Nancy, France, who had noted an exophthalmos of 5 mm.

Operation was performed at Bello Horizonte on December 21, 1939, by Dr.

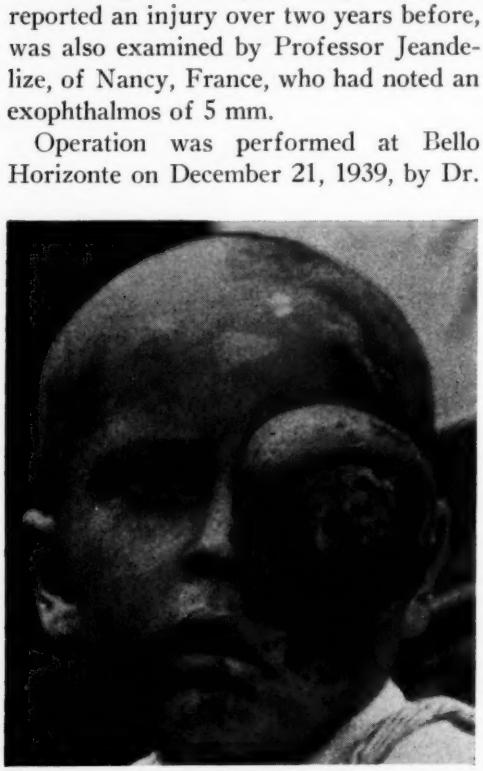


Fig. 17 (Pereira Gomes). Patient, four-year-old boy, in case 13.

Carlos Gama, assisted by Drs. Rivadavia Gusmao and Bayard Gontijo. A tumor of the left optic nerve was encountered, extending from the chiasm to the optic canal, of the size of a hazelnut. It was removed by electrocoagulation by means of a transfrontal craniotomy. The patient died immediately after the operation. Autopsy was not permitted by the patient's family.

Case 13 (1930, Dr. Pereira Gomes). Tumor of the optic nerve, of exceptional dimensions, simulating glioma of the retina, or retinoblastoma. Exenteration of the orbit. Death four hours after operation. Diagnosis: Medulloblastoma (fig. 17).

J. C. E., a four-year-old white boy, native of Itapetininga, State of São Paulo, entered the Santa Casa of São Paulo on March 28, 1940. The family history was negative. His parents were ignorant country people, and they did not bring the child for examination until the tumor of the left eye had attained the enormous size shown in the photograph. General clinical and laboratory examination, including a study of the right eye, were negative. Examination of the left eye revealed a monstrous tumor, with an enormous stretching of the upper and lower lids, invading and literally filling the left orbit. The destroyed eyeball could not be identified in the tumor mass.

Diagnosis of glioma of the retina, or retinoblastoma was made. On the basis of this diagnosis, the futility of any form of treatment was explained to the child's parents who were told that death would be the inevitable result of surgical intervention. In spite of this, they insisted upon immediate operative treatment of the patient. For this reason, X rays of the

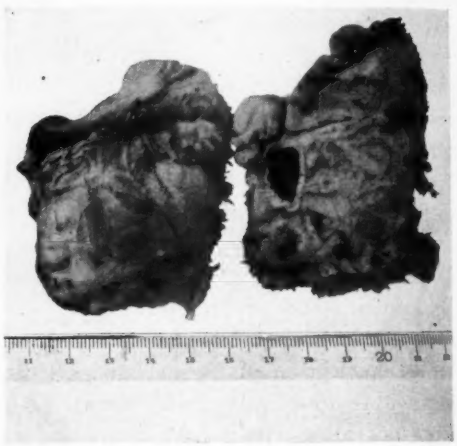


Fig. 18 (Pereira Gomes). Tumor removed in case 13.

skull were not made. The operation, consisting in exenteration of the orbit, was performed on April 1, 1940, under basoformin anesthesia. The tumor filled the orbit, and destroyed part of its lining, through which the cerebral pulsations

could be felt. The operation was completed normally, and the child, after an occlusive pressure dressing was returned to his bed where he received appropriate cardio-tonic injections. Four hours after the operation, he died quietly, after awakening from the anesthetic sleep, in such a manner that the true cause of death could not be ascertained. Was it intoxication from basoformin, or cerebral decompression, or shock from liberated histamine? Autopsy was not permitted.

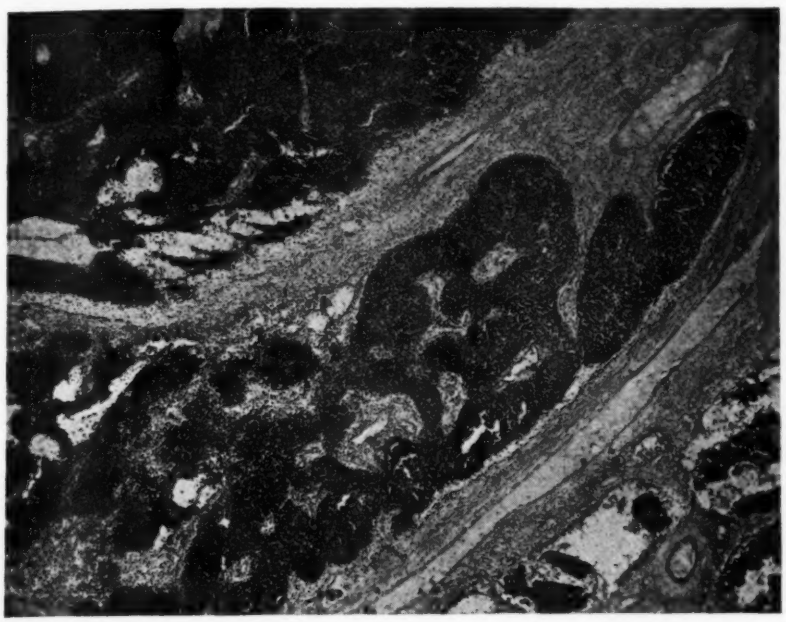


Fig. 19 (Pereira Gomes). Photomicrograph showing large groups and bands of tumor cells infiltrating the connective tissue at the periphery of the tumor. (Hematoxylin-eosin stain.)

The tumor was sent to Dr. J. R. Meyer, of the Biological Institute of São Paulo. My diagnosis was found to have been incorrect. The tumor was one of the optic nerve, and not a malignant glioma of the retina. If the child had not died inexplicably after operation, he might have survived for a long time.

Dr. J. R. Meyer kindly furnished me with the following description:

Macroscopic appearance: The specimen consisted of a large tumor measuring 8 by 5 by 4.5 cm. The anterior part of the growth revealed the external portions of the ocular apparatus; these were thickened and edematous (fig. 18). The other portions of the specimen contained large masses of soft whitish tissues, partially covered by a thin membrane. A superficial section disclosed the atrophic eyeball, measuring 1.8 cm. in diameter. Its walls were corrugated, giving the sclerotic a wavy appearance. Tumor tissue did not invade the interior of the globe. The tumor completely surrounded the eyeball, growing mainly in its posterior and inferior portions. The nerve head and the optic nerve could not be identified.

Microscopic appearance (figs. 19 to 28): Sections obtained from different parts of the tumor showed a cellular tissue made up of large groups, bundles, and masses of small cells, frequently surrounding small blood vessels. The large

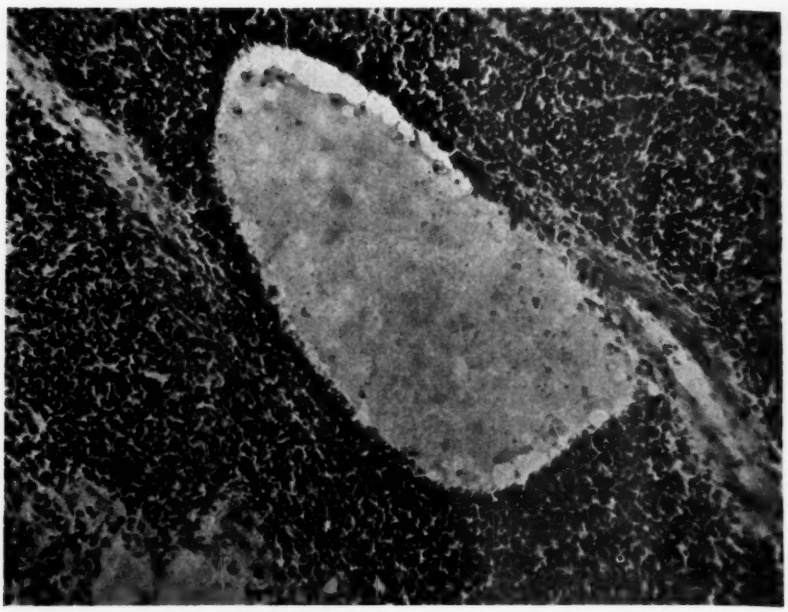


Fig. 20 (Pereira Gomes). A pseudocystic cavity filled with clear fluid and showing no evidences of epithelial lining. (Hematoxylin-eosin stain.)

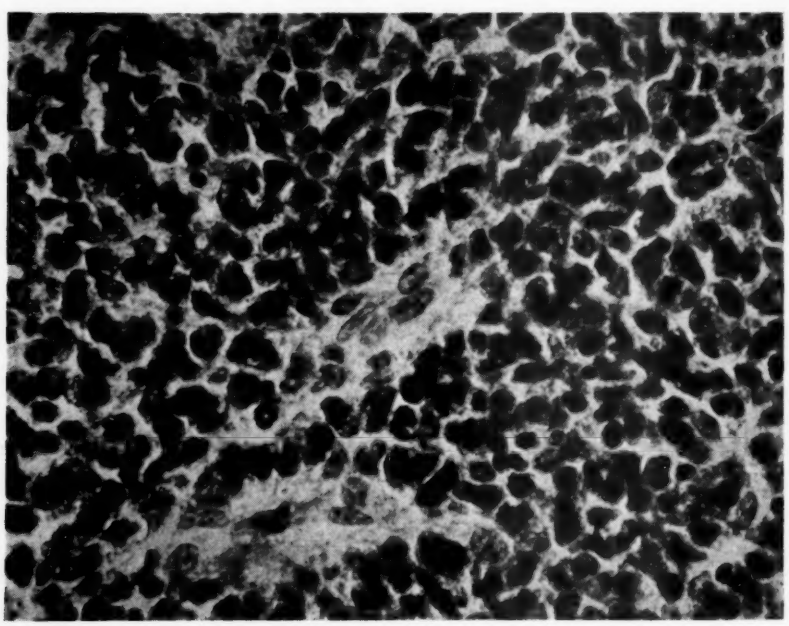


Fig. 21 (Pereira Gomes). Photomicrograph showing the cells of the tumor around two small vessels. These cells are small and are almost entirely represented by oval or elongated nuclei with abundant chromatin. (Hematoxylin-eosin stain.)

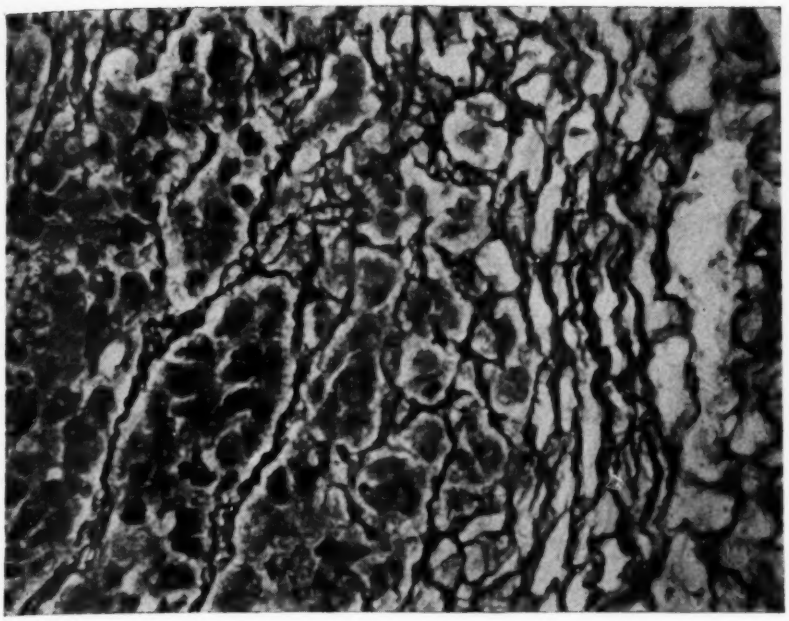


Fig. 22 (Pereira Gomes). Photomicrograph showing the reticulum of the connective tissue at the periphery of a tumor band, invaded by the tumor cells. (Gmöre's silver-impregnation method.)

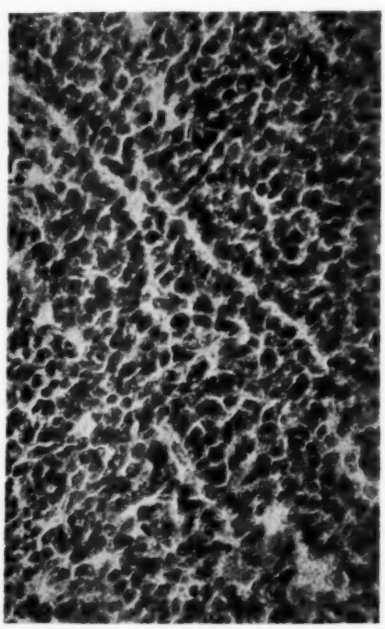


Fig. 23 (Pereira Gomes). Tumor cells showing tendency to form "palisades" on thin connective-tissue septa. (Hematoxylin-eosin stain.)

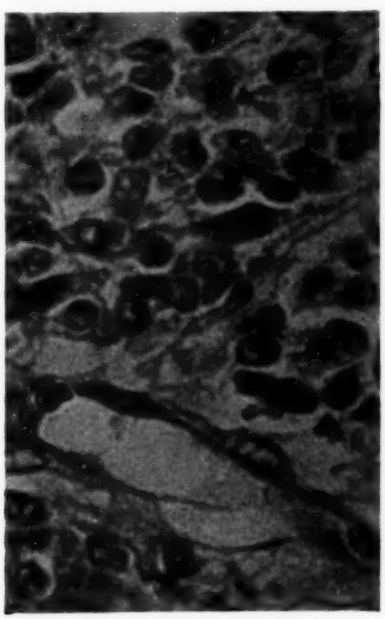
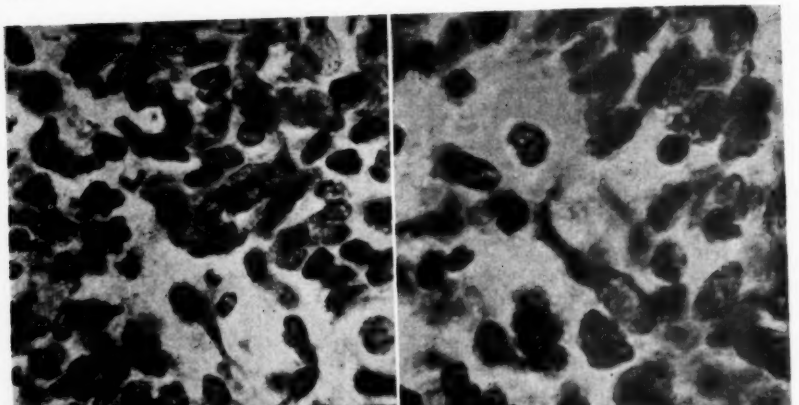
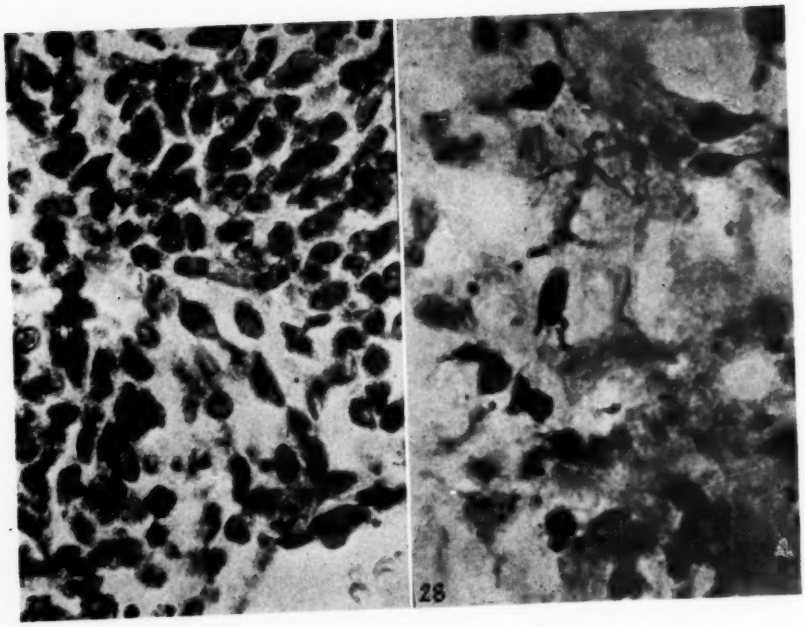


Fig. 24 (Pereira Gomes). Tumor cells showing a small amount of spindle-shaped protoplasm. (Eosin-methylene blue stain.)



Figs. 25 and 26 (Pereira Gomes). Elongated cells having a long cytoplasmic process impregnated by silver, suggesting spongioblasts. (Hortega's fourth variant and Cajal's silver reduced staining method.)



Figs. 27 and 28 (Pereira Gomes). Large cells with very clear nuclei having heavily stained nucleoli, suggesting neuroblasts. (Hematoxylin-eosin stain.)

groups of cells were separated from one another by connective-tissue septa, which appeared edematous in some areas. This tissue was most abundant in the periphery of the tumor, where the infiltrative character of the small cells could be observed. The cells which formed the masses or bundles of tumor were small and made up almost entirely of nuclei. Their nuclei were oval or elongated and rich in chromatin.

Sections stained by the methods of Schultze, Rio Hortega, and Cajal showed a small number of cells with elongated

processes. The cells were suggestive of spongioblasts. In sections stained with methylene-eosin could be seen reduced numbers of large cells containing clear nuclei and intensely staining nucleoli. These cells had the characteristics of neuroblasts. In accordance with these data the tumor was classified as a medulloblastoma.

Origin of the tumor: Three possibilities can be considered:

A. The tumor consists of undifferentiated retinal cells, of the group of retinocytoma or retinoblastoma of Mawas. The following facts are against this hypothesis: (1) the tumor was entirely extrabulbar, no tumor tissue being found within the ocular chambers; (2) nerve cells or neuroglia are not frequent in tumors of this group; according to Bailey and Cushing, in neoplasms of this group, one must encounter occasional nerve cells or neuroglia, or even a tumor composed almost exclusively of neuroglial cells like the angioblastoma retinae of von Hippel.

B. The second hypothesis is that of a tumor arising from medullary cells disseminated via the leptomeninges, infiltrating the soft tissues around the eyeball. This hypothesis is not favored by the clinical history. Tumors arising from medullary cells, spreading along the leptomeninges, are boldly invasive not only in the base of the cerebrum but also along the spinal canal, producing symptoms that were not present in this case.

C. The third hypothesis, supposing that the tumor arose from medullary cells retained in the optic nerve, is one that can be admitted, first, by the retro- and peribulbar development of the tumor and, second, by the embryonic origin of the optic nerve which in the initial period of its development is a continuation of the diencephalon. Undifferentiated cells derived from the medullary epithelium may remain in one stage in the development of the optic canal (canal opticus), and later in the optic nerve, giving origin not only to medulloblastomas but also to medulloepitheliomas, pinealomas, pinealoblastomas, neuroepitheliomas, spongioblastomas, and so forth.

Diagnosis of tumors of the optic nerve

The diagnosis of primary tumors of the optic nerve must be carefully investigated. Although easy, principally because several cases have already been observed and when the two main symptoms, exophthalmos and diminution or loss of vision, have been confirmed, one should not disregard all the elements of symptomatology of this complex nosologic entity, which still today presents some unknown factors not only from a clinical point of view but also from its histopathology.

Let us survey, one by one, the signs, both objective and subjective, which must be investigated.

Exophthalmos: This is the symptom which attracts the attention of the family and of the patient. Von Graefe tried to establish it as a law that the exophthalmos is always forward. This is not always the case; many times the exophthalmos is deviated, now to one side, now to the other, even in advanced examples of these tumors. LaGrange stated (Encyclopédie Française d'Ophtalmologie, v. 7, p. 563): "In fact one never observes, at least in advanced cases, a deviation of the eye toward the internal side." Two of my cases presented this deviation, confirming what has been observed by other observers, among whom are Parsons (five cases) and recently F. A. Davis (two cases). Everything depends upon the size, shape, and situation of the tumor, the gradual and progressive growth of which is always very slow, and without inflammation. The exophthalmos, which is irreducible and nonpulsatile, should be measured

by comparison with the other eye or directly by the exophthalmometer of Hertel.

Disturbance of vision: Diminution and loss of vision are observed early, even before the appearance of exophthalmos, making the diagnosis quite difficult. Rarely, the vision is preserved intact in the presence of a large exophthalmos. Loss of vision is the rule in cases of glioma.

Pupillary reactions: The pupillary reactions depend upon the reduction of visual acuity of the affected eye. The consensual reaction is maintained intact for a long time in spite of total loss of vision.

Ophthalmoscopic signs: These signs consist principally of a commencing papilledema, with or without accompanying hemorrhages and exudates, ending finally in postneuritic atrophy of the papilla, and also in a simple descending atrophy of the papilla when the tumor is located in the orbital funnel. Still, with direct ophthalmoscopy or retinoscopy, a progressive hypermetropia is a sign which is always present, rarely failing to be observed. Knowing that the eyeball is pushed directly forward by the tumor, this sign is easy to comprehend, although little investigated.

Disturbances of motility: As a rule, the motility of the eyeball is not disturbed for a long time, particularly when the exophthalmos is direct. This is contrary to what occurs in exophthalmos due to other causes. The ocular movements are present in all directions, but may be slightly less ample. When the tumor assumes large proportions, the stretched eyelids may be insufficient to cover the eyeball.

Palpation: It is possible, sometimes, but not always, by digital palpation of the orbit between the orbital wall and the eyeball to identify the existence of the tumor, which is mobile and separated from the orbital walls with which it has relations of contiguity only.

Pain: In the great majority of cases, there is no pain. When the tumor, however, is more voluminous adjacent to the globe, compressing the ciliary nerves, pain may be present, at times intolerable.

Growth of the tumor: The tumor has no tendency to penetrate the eyeball; it more frequently takes the direction of the cranial cavity, passing through the optic canal. Even so, there are cases of penetration into the eyeball, such as the one described by Wilson and Farmer (Arch. of Ophth., 1940, March, p. 605). In my case (13) there was involvement and consequent destruction of the globe, an exceedingly rare occurrence.

General condition: While the tumor develops in the orbital cavity, the general health of the patient does not suffer. It is necessary to search for evidences of von Recklinghausen's disease in the patient and his family.

Cerebral manifestations: Intracranial invasion may give rise to headache, personality changes, vomiting, epileptiform seizures, and even paralyses of the limbs.

Radiography: Data from this study are indispensable. The dimensions of the orbit, the condition of the sella turcica, evidences of increased intracranial pressure, and especially a comparative study of the optic canals are to be investigated. It is necessary to compare the two optic canals, because an estimate of the normal diameters of the optic canal (4 mm.) depends on various factors and may be subject to a false interpretation.

Differentiation from secondary tumors: In the diagnosis of primary tumors of the optic nerve, it is necessary to exclude other types of newgrowths which may indirectly involve the nerve; such as, gliomas of the retina, sarcomas of the choroid, cysts and tumors of the orbit and its walls, intracranial neoplasms, and metastatic growths.

Visual field: Data obtained from a

study of the visual field cannot be slighted. The visual field of the involved eye will furnish but little information. It is necessary to investigate the integrity or flaw in the visual field of the healthy eye.

Even with a consideration of all these data, the differential diagnosis often presents serious difficulties, almost impossible of solution, when the tumor is in its early stages, before the onset of exophthalmos.

Benignity and malignancy

The estimation of the degree of malignancy of tumors of the optic nerve has been the subject of many investigations. It is apparent that a single observer, because of the limited number of his cases, will not be able to establish conclusions without a study of the cases reported in the world's literature. Even in cases of partial extirpation of the tumor, orbital recurrences are rare, as are also the complications consequent upon intracranial invasion. Patients who have survived from 10 to 20 years are numerous. It is very difficult to find records of patients who have kept in touch with their surgeons for a long time. Of the cases from Brazil, one patient (case 3) is living and well 21 years after operation, and another (case 5) was in good health 8 years after operation. In any event, the prognosis as regards life in these tumors is good, notwithstanding the impossibility of avoiding surgical intervention. Left to themselves, these growths finally invade the cranial cavity, or destroy the orbital walls, or indirectly cause a loss of the eyeball, resulting in a series of complications capable of causing the death of the patient. One thing that causes confusion in the understanding of this problem is the difference in concept of the benign or malignant nature of the tumor between the surgeon and the pathologist. For the former, an extirpated tumor is benign which does not recur, which does not produce metastases, which does not endanger the life of his patient, which manifests hardly any local invasiveness; these facts are evident and admitted by all observers in tumors of the optic nerve. For the pathologist, the criteria established are different, since he bases his opinion upon the morphologic aspect of the growth, upon its cellular structure, upon its proliferation, upon its size, upon the disposition of its component elements, and finally upon its ability to invade neighboring tissues by continuity or by means of metastases.

With these considerations, when the tumor extends through the optic canal and invades the cranial cavity, I believe that the malignity continues to be local because the neurosurgeon, called in and acting in time, will almost always be able to resolve the most difficult problems, as was seen in case 11 in my series.

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Clinical classification

The classic topographic classification of tumors of the optic nerve into intradural and extradural, or better, according to Verhoeff into intraneural or extraneural, should be conserved, although from an histopathologic point of view this may be criticized. This classification is clear and didactic. The glioma, which is the most frequent tumor, can, notwithstanding its intraneural origin, invade the pia and continue involving the intervaginal spaces, in the same way as the endothelioma can start extraneurally or intraneurally.

From the clinical and didactic point of view, the intradural tumor, distending and thickening the external sheath of the

nerve, presents the characteristic form of a sausage; the extradural tumor is usually not confined by the dural sheath and, adapting itself to the shape of the orbit, takes the form of a pear, with its largest part lodged against the eyeball. Whatever the shape, the question does not have great importance, since there is little reason to condemn this classic classification.

Histopathologic classification

I am not a pathologist, and my opinion has, moreover, no authority. I must say that even in this field, the opinions of those competent to have them are far from being in accord. I accept the classification of Hudson (1912). Tumors of the optic nerve belong in three categories, according to their histologic nature: *gliomas*, much more frequent, arising from the nerve trunk; *endotheliomas*, much more rare, arising from the arachnoid or from the dural sheath; and *fibromas*, still more rare, derived from the dural sheath.

Relations between the tumors of the optic nerve and von Recklinghausen's disease

The relationship between these tumors and von Recklinghausen's diseases has been long and carefully observed by writers. The literature concerning this subject has been admirably reviewed in the work of Davis, which contains a complete summary of the pathology involved, as described in the publications from those of Michel in 1873 to those of recent date.

Almost all authors consider as a simple coincidence the findings of signs of von Recklinhausen's disease in cases of tumors of the optic nerve and not as a manifestation of the same syndrome. This is mainly due to the knowledge that the optic nerve does not resemble the peripheral nerves, from which it differs in its sheaths and in its sustaining tissue.

Davis has brought this problem to a focus, to his great credit, by calling the attention of ophthalmologists to this subject and by advising a systematic investigation, in patients with tumors of the optic nerve, of all the signs of von Recklinghausen's disease, specifying soft skin nodules, café-au-lait spots, possible lesions of the choroid, ciliary body, and iris in buphthalmus, skeletal deformities, and neurofibromatosis especially of the eyelids and orbital nerves.

It is the first time that an ophthalmologist considers tumors of the optic nerve, chiefly those of the glial type, as one of the manifestations of this interesting syndrome, thus opening a field for future valuable clinical investigations.

Methods of surgical treatment

From a study of the history of tumors of the optic nerve, two features can be well established from a surgical viewpoint. First, these tumors develop most frequently in the orbital portion of the nerve and do not always extend to the cranial cavity; second, even in cases of incomplete extirpation in this region, recurrences are very rare. This being the case, I believe that orbital intervention is not palliative but often curative. I do not consider it advisable to intervene at the beginning by transfrontal craniotomy.

Woods, of Baltimore, discussing the work of Davis, takes the opposite viewpoint, preferring the transfrontal route. I agree that this procedure may be advisable for other kinds of deep orbital growths, but not for tumors of the optic nerve, especially intradural gliomas. I cannot understand why it is necessary to open the cranial cavity to extirpate a tumor which is almost always benign and which is exclusively situated in the orbit.

Among the cases from Brazil, described above, there had not been a recurrence observed after orbital intervention

in cases 1 (2 years), 3 (21 years), 5 (8 years), 6 (1 year), 8 (1 year), and 10 (1 year). The two autopsied cases of Dr. W. E. Maffei, in which the tumors encountered were purely orbital, bear out this feature.

From these explanations, I believe that tumors of the optic nerves should be extirpated: (1) with preservation of the eyeball, whenever possible; (2) by enucleation of the eyeball followed by extirpation of the tumor; and (3) by exenteration of the orbit, when the tumors invade the orbital cavity.

In the technique of extirpation of the tumor of the optic nerve with preservation of the eyeball, I have been satisfied with the procedure of Lagrange, the external orbitotomy of Rollet, and the recent method of Davis. I am not in favor of incising the tumor and evacuating its contents, by the technique of Golovine. Nor do I approve of the original technique of Herman Knapp, because the way of approach to the orbit in its superonasal region, which he advised, is much less practical and much more subject to complications. Krönlein's operation, which is preferred by many authors, appears to me to be unnecessary in these cases.

When there is evidence that the tumor has already invaded the cranial cavity, transfrontal craniotomy should be first employed, followed later by an orbital approach, as described in case 11.

These interventions should not be simultaneous, that is to say they should not be performed at the same operation. In regard to the new technique of removal of the bony lining of the orbit and of the optic canal, I can give no opinion, because it has not yet been employed in Brazil, as far as I know. Since this removal as well as transfrontal craniotomy are delicate procedures, and in the province of the neurosurgeon, they are not advisable for ophthalmologists to undertake.

297, rua Maranhão.

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Discussion

Dr. Frederick Allison Davis (Madison, Wisconsin): I am honored by the invitation to discuss Dr. Gomes's excellent paper.

He has assembled and made a very comprehensive study of the case records of 13 patients, which is indeed a large number when one considers the comparative rarity of these tumors. His paper is accompanied by excellent photographs of

the material discussed. Unfortunately, a copy of his paper was not available to me until yesterday, so that it has been impossible for me to make as complete an analysis of his case reports as they deserve.

Dr. Gomes's observations and comments concerning the diagnosis and clinical manifestations of primary tumors of the optic nerve are especially thorough; I feel he has justly directed attention to some erroneous statements which appear in the literature.

He retains the classification originally suggested by Hudson, and amplified by Verhoeff; namely, (1) gliomas, (2) endotheliomas, (3) fibromas, or fibromatosis. It is my belief that the latter group (fibromas), which are extremely rare, should be eliminated from this classification. They probably belong to the group of so-called "pseudo-tumors," as suggested by Verhoeff.

In the series which the essayist reports, by far the greater number of the tumors were gliomas, which is in accord with the statistical data published by various authors. I found approximately two thirds of the cases on record were gliomas, while about one third were probably endotheliomas. Much confusion in the pathological diagnosis of the tumors appears in the earlier literature, since many of the gliomas were erroneously regarded as sarcomatous in nature. Hudson and also Verhoeff have been largely responsible for clearing up many of the disputed points in this connection. More recently, newer staining methods have clearly demonstrated the glial nature of the majority of the tumors.

The relationship of tumors of the optic nerve and von Recklinghausen's disease has been stressed by Dr. Gomes, and it is particularly gratifying to me that he agrees with the views I have previously expressed in this regard. This was the main theme of a paper recently presented by me before the Eye Section of the American Medical Association. My convictions regarding the importance of this relationship have been strengthened by three additional cases, all in young children, which have been brought to my attention by colleagues, since the publication of my paper. Two of these cases have been reported. I had the privilege of personally examining two of the patients through the courtesy of Dr. Rodman Irvine, one of which was reported in the Archives of Ophthalmology in 1939 by Rand, Irvine, and Reeves. In this patient, the cutaneous lesions, which consisted of coffee-colored spots, were either overlooked or disregarded by the authors, since their significance was not at first recognized. The second patient had a proptosis of one eye, numerous coffee-colored patches in the skin, and bony changes which, upon X-ray study, were regarded as characteristic of those at times seen in von Recklinghausen's disease. This child had not been operated on at the time I saw him, nor has the case yet been reported to my knowledge.

The third patient referred to, was a boy of three years, reported by Tanner and Hertzog in the Wisconsin Medical Journal of January, 1940. This patient had no cutaneous nor other lesions associated with von Recklinghausen's disease. However, at my request, the authors reëxamined him and members of his family. They wrote me "There were no coffee-colored patches on the body of the patient or on his father or mother, but they were present in two sisters, and also in a paternal aunt, grandmother, and great-grandmother of the child." Through the kindness of Drs. Tanner and Hertzog I made extensive histopathologic studies of the specimen removed by them, which included the globe and most of the optic nerve and tumor. Differential staining

revealed a fairly advanced tumor of the glioma type. These cases strikingly illustrate a point which I stressed in my paper; namely, that in many of the optic-nerve tumors reported in the literature, the associated lesions of von Recklinghausen's disease may have been completely overlooked. This oversight is understandable since the theory of a relationship of these tumors and von Recklinghausen's disease had not been definitely established and had in fact been dismissed or vigorously denied by many outstanding authorities in this field of investigation. Further confusion has arisen from the fact that the tumor of the optic nerve may in some instances prove to be the sole manifestation of the disease. However, if von Recklinghausen's signs are present in either members of the family or relatives, the diagnosis should be unquestioned. Unfortunately, from an etiologic standpoint, incomplete physical examinations have rendered many of the case reports valueless.

With regard to treatment, I am in complete accord with the essayist. I believe some method of retrobulbar removal of the growth, with preservation of the globe, should be the operation of choice. It can be safely carried out in most cases if the tumor has not become too large. I prefer this approach to the Krönlein procedure, since it is simpler and less disfiguring. Dr. Gomes informs me that he is also of the same opinion, although through an error he was misquoted in the abstract. He prefers the Lagrange method, which is similar to the operative approach that I have employed. If the growth is extremely large, enucleation with partial removal of the orbital contents may be necessary. If there is definite evidence of intracranial extension the transfrontal operation should be the logical approach in those cases which were considered operable. Unfortunately, gliomas of the optic nerve, which are the largest group, may be multiple. They may extend into, or from the chiasm, or they may exist as independent lesions in this or other parts of the brain. They are, therefore, frequently inoperable from the standpoint of complete extirpation, as has been pointed out by Cushing, except where they appear as an isolated lesion in the optic nerve.

I concur in Dr. Gomes's statement that craniotomies should be reserved for neurosurgeons, but I believe the operation on the orbit, including exenteration, should be performed by ophthalmologists.

Dr. Gomes is to be congratulated upon his very valuable contribution.

A NEW APPROACH TO TESTING THE EYES OF SCHOOL CHILDREN*

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The problem of detecting ocular difficulties sufficient to impair the achievement or health of the school child has been recognized for many years. Under ideal conditions each pupil should receive a professional eye examination yearly, but this has never been possible because of the insufficient number of trained examiners available. The problem has been met in part by a yearly program of visual-acuity testing with the Snellen chart, but it is not very satisfactory because the test fails to screen out many patients with visual insufficiency who should be found and given glasses or treatment. The Snellen test misses many cases of hypermetropia because the vigorous accommodation of school children usually enables the hypermetropic ones to clear their vision, at least long enough to read the test types and pass the test. It also fails to pick up cases of muscular imbalance and defects of binocular vision. To estimate the efficiency of the Snellen test as an instrument for detecting eye trouble among school children the cases of 500 school pupils with eye difficulties sufficient to warrant the use of glasses or treatment were reviewed. Each pupil included in the group had received a professional eye examination and either glasses or treatment had been prescribed. Fifty-four percent of the cases tested 20/30 or poorer and would have been picked up by a Snellen test used for screening, while 45 percent tested 20/20 or better, notwithstanding their ocular trouble, and would have been missed in a school-testing program employing the Snellen test.

Some means of detecting the 45 percent missed by the Snellen test is highly desirable, and it was toward that end that work was started on the development of an improved screening test for the use of teachers. It was recognized that such a test must fulfil at least three major requirements:

1. It must be much more discriminating than the Snellen test. 2. It must be so simple that any teacher may give it successfully with the help of a few directions. 3. It must not require too much time or equipment for administration.

Several simple tests were brought together and combined into an experimental unit that was administered to school children in different communities. The responses to these tests were studied and the inefficient ones, together with those that were difficult for teachers to give, were eliminated. Among these may be mentioned the radiating line or "Clock-chart" test for astigmatism. Although it is of undoubted value to the trained examiner, teachers were generally unable to get good results with it. Various stereographs were used for screening out muscular imbalances but were not very successful and gave teachers considerable trouble. Finally one was developed that will be discussed in a later paragraph. Several other stereographs were tried for testing fusion and binocular vision. An attempt was made to test for deficiencies of fusion for different sizes of type, but it was found that the community of function of these tests was so great that all but one of the stereographs were discarded permanently.

There is so much difference of opinion as to the amount of hypermetropia that calls for correction that the selection of the proper lens power for what later came

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to be called the "lens test" presented a difficult problem. Lenses of plus .50, plus .75, plus 1.00, and plus 1.25 D. were tried and discarded.

It was suggested that one of the subtests be directed specifically to screening at the reading distance, but a review of 200 pupils tested at 20 feet and again at the reading distance revealed the following facts: (a) high correlation between the results of distance- and near-screening tests among hypermetropic pupils; (b) low correlation between the results of distance- and near-screening tests among myopic pupils; (c) very high percentage of myopic pupils screened out by the visual-acuity test at 20 feet. For these reasons a separate subtest to be administered at the reading distance appeared to be superfluous.

The present battery of tests includes the following subtests:*

1. *Visual-acuity test.* The Snellen test was used to screen out pupils with eye trouble producing low vision, such as myopia, amblyopia, and the like. This particular visual-acuity test was selected for a number of reasons, the more important of which are: (a) It is virtually the standard visual-acuity test, and is widely used in ophthalmology. (b) It is used in many schools, and many teachers are already familiar with it. (c) It is very simple to administer. Children who are unable to read the 20-foot line at 20 feet fail the test. Some schools have adopted 20/40 as the level at or below which the test is scored as failed, but the author considers this too low. Further to simplify the administration of the test a card was prepared with one 20-foot line of letters and one 20-foot line of "E" symbols, the choice of which line to use being determined by whether or not the children to be tested knew the names of the letters. Not more than two symbols on the line may be failed if the test is to be scored as passed.

2. *Lens test.* This is a repetition of the visual-acuity test, except that the child being tested reads the letters (or recognizes the "E" symbols) while looking through a plus 1.50 D. sph. with the eye under test. It is evident that this lens will impair the ability to see the card clearly when used over emmetropic or myopic eyes, yet will permit the hypermetropic eye to see as well or better than without it. The purpose of the test, then, is to screen out important cases of hypermetropia. The test is failed if the child gets the same or a better score than he did in the visual-acuity test.

3. *Coördination test.* This test is made with an ordinary hand stereoscope and a stereograph that presents a rectangle to the left eye and a chicken to the right eye. The proximal edge of the card carrier is set 4½ inches from the front surface of the stereoscope lenses, and it is recommended that this position be marked for convenience in setting the instrument. The rectangle is 1.5 by 4 cm., its dimensions having been determined by noting the apparent deviation of the chicken in cases of heterophoria which received remedial treatment after professional eye examination. The limits of the rectangle enclose the area of variation among cases which, in the course of an eye examination, were passed by the ophthalmologist. This test is failed when the chicken appears to the child to be outside the rectangle (or yard). Other failure responses are, "The chicken runs in and out of the yard," or "I see only a chicken (or a yard)."

4. *Fusion test.* This test of binocular vision is also made with a hand stereoscope but with a stereograph that presents a star and a crescent to each eye, thus:

* Material for making the test and a manual of instructions are now supplied by the World Book Co., Yonkers, New York.

* C C *. The card is placed in the carrier and it is set at the position described in the previous paragraph. The child is asked what he sees. If he does not fuse the * C C * into * C * he is permitted to slide the card carrier back and forth two or three times in an effort to fuse the pictures. The test is failed if the pupil is unable to fuse the pictures to * C *.

Two general rules have been laid down for the guidance of teachers giving the test to their pupils: 1. A single failure on any subtest constitutes failure of the entire battery. 2. Children who fail the test should be reported to the school physician, school nurse, or parents, according to the accepted procedure in the school where the test is given.

There is a strong tendency among many lay people who administer screening tests to attempt to diagnose difficulties disclosed by the testing, and so it is recommended that the terms "Passed" and "Failed" be used in connection with the test results. Teachers and other lay users should be instructed that the only interpretation to be placed on a failure response is that the child should be referred to the proper authorities for eye examination. They also should be informed that passing the test does not mean that the child is free from eye trouble but that he is only somewhat less likely to have a serious amount of it than are the others. The common medical terms, "Positive" and "Negative" usually mean to the teacher just the opposite of what is meant by the physician. To the teacher the term "Positive" is equivalent to "Passed," and "Negative" is equivalent to "Failed." This probably came about through the general practice of marking standardized educational and psychological tests with a "Plus" for success and a "Minus" for failure. Physicians working with educators should avoid these terms and keep in mind this possibility of misunderstanding.

One of the criteria of any good test is that it measure consistently. Its reliability depends on how well it agrees with itself when repeated. In order to determine the reliability of the test battery it was administered twice to 516 pupils, and the results of the two administrations were compared. The results agreed in 96 percent of the cases.

The validity of any screening test for ocular difficulties is best determined by a comparison of the results of the test and those of a professional eye examination. In how many of the cases indicated by the screening test as needing attention to the eyes do ophthalmologists find trouble sufficient to warrant treatment? This proportion is sure to vary with the individual examiner because of the wide variation in personal judgment and the lack of any mathematical standards for correction or treatment. It is probable that there can never be such mathematical limits because of individual differences in patients and their responses to ocular difficulties. With this limitation in mind the scores of 131 pupils who had also received professional eye examinations were compared with the oculist's results as to the presence or absence of eye trouble sufficient to require glasses or other treatment. The test results agreed with those of the oculist in 95 percent of the cases.

It was learned from a test-by-test study of 278 cases that a combination of the visual-acuity test and the lens test screened out 81 percent of the cases screened by the entire battery. The visual-acuity test picked out 62 percent and the lens test an additional 19 percent in this group. This suggests that these two tests may be used alone when time does not permit the use of the full battery, thus doing a reasonably good job of screening

in a minimum of time.

These statistics are presented to help in the evaluation of the new test battery but no effort has been made to make it unassailable statistically. Throughout the work of developing the test the emphasis has been entirely on the human and social values involved and the aim of the work has been to produce a test that will pick out more cases needing eye care than can be accomplished with the Snellen test now so widely used. The author thinks that this end has been attained but is continuing his study of the problem with a view to further improvement in the test.

SUMMARY

A new test for screening out school children with important eye trouble is described. The purpose of the test is to provide a more efficient instrument than the Snellen test now so widely used in the schools. Statistics on the inadequacy of the Snellen test are given, development of a new test is discussed, the present test battery is described, and a statistical consideration of its reliability and validity is presented. Five hundred sixteen cases are involved in the study.

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THE RETINA AND INTRAOCULAR TENSION DURING PROLONGED INSULIN COMA

With autopsy eye-findings

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A previous paper[1] reported the retinal findings in a series of 70 patients with functional psychosis who had received insulin-shock therapy. In it was given a complete review of the literature dealing with the fundi in untreated mental patients, and the eyegrounds and intraocular tension of treated patients. This paper should be referred to. Since it was written, Powell *et al.*[2] have made observations of the eyes during insulin coma. They conclude that (a) the fundus and optic disc become pinker, the veins becoming engorged and the arteries relaxed; (b) the vitreous becomes hazy; (c) the intraocular tension increases but may subside during the coma; and (d) all these changes disappear shortly after the administration of glucose. Unfortunately, they did not make blood-sugar determinations and studied only two cases during one period of hypoglycemia.

Inasmuch as the retina is derived from, and is histologically similar to, the brain, my first study was made to see what changes occurred in it. Pathologic changes occur in the brains of experimental animals suffering hypoglycemic convulsions or comas of several hours' duration. Comas of short duration which are terminated by the intravenous injection of glucose do not result in brain alteration. In humans the bulk of work has been done on the brains of patients who have died after comas of many hours or days. These brains show extensive degenerative and vascular changes.[3]

The retina is similar to the brain in still other ways. According to Himwich *et al.*,[4] Lennox,[5] and Wortis and Goldfarb[6] the brain consumes glucose almost exclusively. It has a respiratory quotient of one. In ordinary insulin coma and irreversible coma with hyperglycemia the brain's metabolic rate is definitely decreased.[4b] Grieg *et al.*[7] report that the retina most nearly resembles the brain in its consumption of glucose, and Dickens and Simer[8] say the retina's respiratory quotient is one. In fact the latter state "the retina occupies a quite exceptional position among all animal tissues since it has the highest respiration and highest anaërobic glycolysis of any tissue yet studied."

Adler[9, 10] states that the retina and brain have the highest rate of glycolysis. In an experimental study on cats he found the average blood sugar 135 mg. percent and the sugar content of the aqueous and vitreous 113 mg. percent and 64 mg. percent, respectively. He reports that the retina's glycolytic activity is almost double that of any other ocular tissue. In addition, he says the retina surrounds two thirds of the vitreous so that sugar getting to the vitreous from the choroidal or retinal circulations must first be exposed to its glycolytic activity. Consequently the sugar content of the vitreous is lowest. Furthermore, the sugar concentration is lowest near the retina and higher anteriorly toward the iris. Lindeman[11] says the retina is one of the most actively respiring tissues. Its metabolism compares quite favorably with that of the brain in frogs.

My first study showed there were no retinal changes in patients sustaining routine insulin coma. I am reporting now on the eyes of a woman who died after 10 days of irreversible coma. Study of this

case had a five-fold purpose; namely, comparison of (a) the fundus with that of patients surviving treatment; (b) the ophthalmoscopic findings with the microscopic; (c) the retinal histopathology with that of the brain; (d) the intraocular tension with those reported for routine comas; and (e) correlation of the intraocular tension with the blood and spinal pressures.

Anamnesis and clinical history

The patient was a 40-year-old, well-nourished, Irish female, weighing 139 pounds, who was admitted to Central Islip State Hospital on June 12, 1939. After graduating from public school she stayed at home because "she was always a home girl who had few friends." Her marked introversion became worse, so that during the seven years before her admission she barely talked to family members and became progressively deafer.

The family, however, found her easy to manage until two weeks before her admission when she began to have auditory hallucinations. She thought people talked about her, and harbored persecutory delusions. She became apprehensive and agitated, trying to leave home during the night. Hospitalization became imperative.

On admission, physical examination was essentially negative. Her blood pressure was 140/100. Both ear drums were thickened and retracted, but the type of deafness could not be determined because of her uncoöperative nature. The blood Wassermann test was negative.

Preceding and throughout her insulin treatment the patient's behavior remained about the same. She was inaccessible, tense, and perplexed. Frequently she appeared depressed, agitated, and fearful. She expressed numerous paranoid ideas, and admitted auditory hallucinations of a threatening character. No visual hallucinations were reported. Sometimes she was resistive and uncoöperative. Mainly the patient was seclusive and idle on the ward. Her condition was classified as a case of Dementia praecox, paranoid in type.

On January 12, 1940, therapy was begun with 15 units of insulin given at 7:00 A.M. She usually went into coma at the end of the third hour or during the fourth hour after injection, and was allowed to stay in for periods ranging from 20 minutes to 2 hours and 10 minutes. Most of her comas lasted well over an hour, and were interrupted by gavage with sucrose solution. Sometimes this had to be implemented with glucose intravenously. One hour and 15 minutes after receiving 50 units as her twenty-fifth treatment a generalized urticaria developed. She was given sucrose and the rash disappeared 2½ hours later. After this, coma could be produced only by increasing the dosage of insulin, so that on March 1st she was getting 125 units. In all she received 2,335 units of insulin in 37 separate treatments given five times a week. The patient had no convulsions but experienced 26 comas.

At 7:19 A.M., on March 7th, she received 125 units of insulin intramuscularly. At 8:15 her skin was cold and clammy and she became restless by 8:30. She had twitchings of her head and extremities at 8:40, and perspired freely by 9:00. Her pulse rose to 120 at 9:45 and she was reported in coma at 10:00—in the middle of the third hour after injection. She was tube-fed 140 gm. of sucrose at 11:05, and received 100 c.c. of 33-percent glucose intravenously at noon.

Her respirations became rapid and irregular and her blood pressure dropped to 95/80. She was placed in shock-position and given one ampule of coramine intramuscularly. Thereafter she received in-

travenously 100 c.c. of 33-percent glucose at 1:00 P.M., and 100 c.c. of 50 percent glucose both at 2:45 and 7:00 P.M. In addition she was tube-fed large quantities of orange juice, but aspirations showed much residue. The Babinski sign was positive bilaterally, and stretching movements and twitchings of the face and extremities were prominent. Decerebrate rigidity was noted frequently.

glucose in saline as well as gavages of orange juice and egg-nog which she retained well. Up to the day before she died heart sounds remained good, pulse rate fluctuated between 80 and 160, reaching the latter figure toward the end, and her blood pressure ranged from 115/75 to 150/110. Her temperature ranged between 99.4 degrees and 104 degrees, mounting to 107 degrees on the last day.

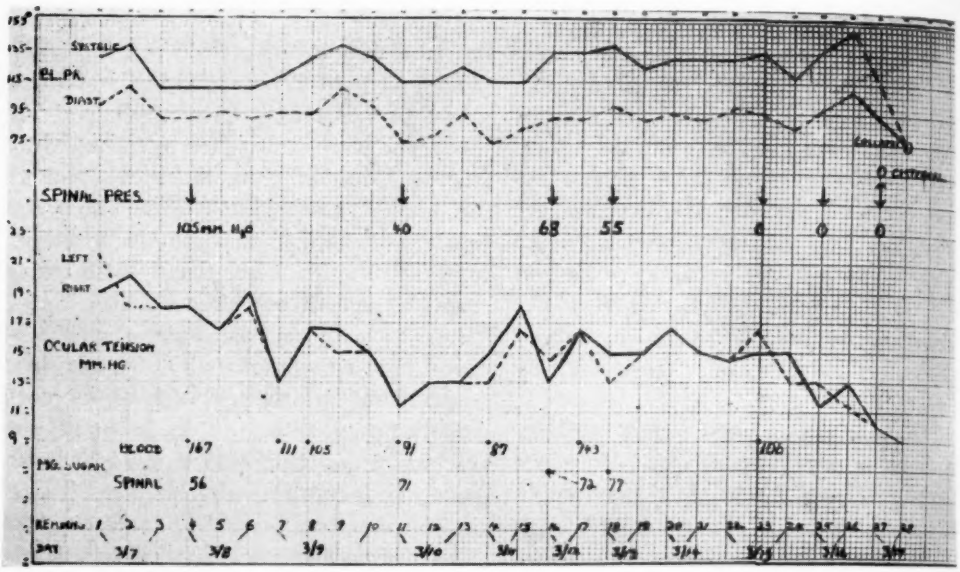

Fig. 1 (Gralnick). Graph showing the relation of intraocular tension to blood and spinal pressures and sugar levels.

The patient had suffered a precipitate coma. By the next day it was definitely irreversible. Her coma had lasted two hours before she first received intravenous glucose; she had a high temperature (103.6 degrees), rapid pulse (118), and respirations (30), and in addition to muscular twitchings she vomited some tube-feedings. Wortis and Lambert[12] report such findings as typical of irreversible coma.

The patient stayed in coma to the time of her death. There was no sign that she would rally. Nutrition was maintained by frequent clyses and infusions of 5-percent

As a rule, respirations were regular and varied from 24 to 40. She perspired very freely and eliminated well, though incontinent. The Babinski continued to be positive bilaterally. Results of blood chemistries and spinal-fluid pressures are shown on the chart (fig. 1).

About 18 hours before death she went into a rapid decline. Her pulse increased in rate, becoming weak and thready, and respirations became rapid and labored. Her blood pressure dropped precipitately, so that six hours before death it could not be obtained. She perspired profusely and had frequent, watery, yellow stools.

All extremities became cold and cyanotic, and her temperature gradually rose to 107°F. Breath sounds were clear in both lungs. The patient died 10 days and 6 hours after coma began.

Technique of Study

Throughout her coma the patient's pupils were maintained in a semidilated condition with 2-percent homatropine to make study of the fundus easier. Ophthalmoscopic examination was done first, careful search being made primarily for retinal hemorrhage and optic-disc injection or edema. The patient was then placed in the supine position and the blood pressure read. Following this three intraocular-tension readings were made with the Schiötz tonometer holding a 7.5-gm. weight. The average was taken as the tension for the moment. This procedure was followed morning, early and late afternoon, and sometimes in the evening. During the night the patient was not disturbed. Spinal-pressure readings were made in the morning shortly after the intraocular tension was taken, and the blood sugar was determined at the same time.

Findings

Fundus. Up to the time of death ophthalmoscopic findings were negative except that there were moderately dilated veins on the last day. The retinae showed no hemorrhages, exudates, nor pigmentary changes, and the discs remained normal in outline and color. The vessels maintained their normal ratio in caliber.

Intraocular tension. Reference to the graph will show that the intraocular tension remained low throughout the coma. It ranged from 21.4 to 13.0 in the left eye, and from 19.0 to 11.4 mm. Hg in the right eye, and declined to 9 mm. Hg 1 hour and 15 minutes before death. The intraocular tension of the eyes paralleled each other closely and remained more or less on an even plane until four days before death when a gradual decline set in.

There was no relation between the blood pressure and intraocular tension, the latter remaining low despite a consistently high diastolic pressure. About 18 hours before death vascular collapse set in. It is indicated on the graph by the acute drop in the blood-pressure curve after the twenty-sixth reading. At 9:15 A.M., 6½ hours before death, the blood pressure could no longer be obtained, but the intraocular tension at this time was 10 mm. Hg, and 1 hour and 15 minutes before death 9 mm. Hg. At the moment of death intraocular tension could not be measured because the eyes were too soft.

The graph shows that there was no direct correlation between the spinal pressure and intraocular tension. However, in the four instances that a spinal pressure could be obtained the intraocular tension fluctuated with it. Thus, when the spinal pressure was 105 mm. water the intraocular tension was 18 mm. Hg; when 40 mm., the eye tension was 11.4 mm.; when 68 mm., the tension of the left eye was 14.6 mm., and 13 mm. when the spinal pressure was 55 mm. The zeros on the graph indicate unsuccessful attempts to register the spinal pressure. In these a few drops of fluid could be obtained, but none would rise in the manometer. A cisternal puncture was attempted on the morning of death but no fluid was obtained. It should be noted that during these three days the ocular tension slowly declined, and at autopsy little spinal fluid was found in the ventricles.

The intraocular tension remained uniformly low despite normal or elevated sugar levels in both the blood and spinal fluid.

One other finding is worthy of mention. Forty-five minutes before death the eyes showed rapid, synchronous, oscillatory

movements in the horizontal plane for about one-half hour. The oscillation was no more than 2 mm. in either direction from the mid-point, at which the eyeballs seemed to be fixed. This movement sometimes stopped momentarily on expiration, but with no regularity.

Autopsy report

The post-mortem examination was reported by Dr. Reider Trygstad of Central Islip State Hospital, as follows: The autopsy was begun 45 minutes after death. General external examination revealed a well-developed white female. The brain weighed 1,370 grams. It was edematous and the sulci were shallow and narrow. The meninges were transparent and had markedly congested vessels. The basal arteries were decreased in caliber. There were no areas of softening or atrophy. The ventricles were smaller than normal and contained a diminished amount of fluid.

The chest cavity was negative and the lungs were congested at their bases. The heart weighed 340 grams and was uniformly dark red. The aortic valve measured 5.5 cm. and the pulmonary 6.5 cm. in circumference. The abdomen showed the serous linings to be smooth and glistening. The adrenals were of average size, and showed congestion of the medullae. The remaining abdominal organs were essentially negative. The eyes were placed in Zenker's solution immediately after removal.

Microscopic examination of the brain: Nissl stain.

This was reported by Dr. Armando Ferraro of New York State Psychiatric Institute and Hospital and Dr. Max Gold of Central Islip State Hospital through collaboration of their respective pathology laboratories, as follows: In the meninges there was a considerable amount of congestion which extended within the cortex and white substance. The veins were generally the ones involved, the dilatation being very pronounced. In the external layers of the cortex, the blood vessels were often seen entering from the meninges and disclosed thickening of their walls. Some of the blood vessels could be followed up to the second and occasionally to the third layer. In addition to these individual long blood vessels, there were, particularly in the lamina molecularis, numerous small blood vessels, disclosing also thickening of their walls. The thickening of the walls was at the expense of the intima in the very small blood vessels and of the outer layers and the intima in the medium-sized ones. The endarteritic process was found also here and there in the white substance. As far as proliferation of blood vessels was concerned, there was a certain amount of newly formed blood vessels, but this neoformation was definitely less pronounced than the one noticed in other cases of insulin encephalopathy.

The nerve cells in the various layers of the cortex were still present in large number, sufficient to preserve the normal cytoarchitecture. There was, however, a certain rarefaction of nerve cells distributed all over the various cortical layers. Here and there, cortical areas were found in which the cytoarchitecture was somewhat disturbed, and other areas, much less numerous, in which the disturbed lamination was quite pronounced (figs. 2, 3). In the cortex, generally speaking, one encountered a more pronounced pathological process in the lamina molecularis where the vascular component of the pathological process was more prominent. In the remaining layers of the cortex, nerve cells were seen undergoing various degenerative changes, mostly chromatolysis. Degenerative process in the nerve cells led in certain areas to the severe type of degeneration, and remnants of nerve cells and shadow cells were seen here and there.

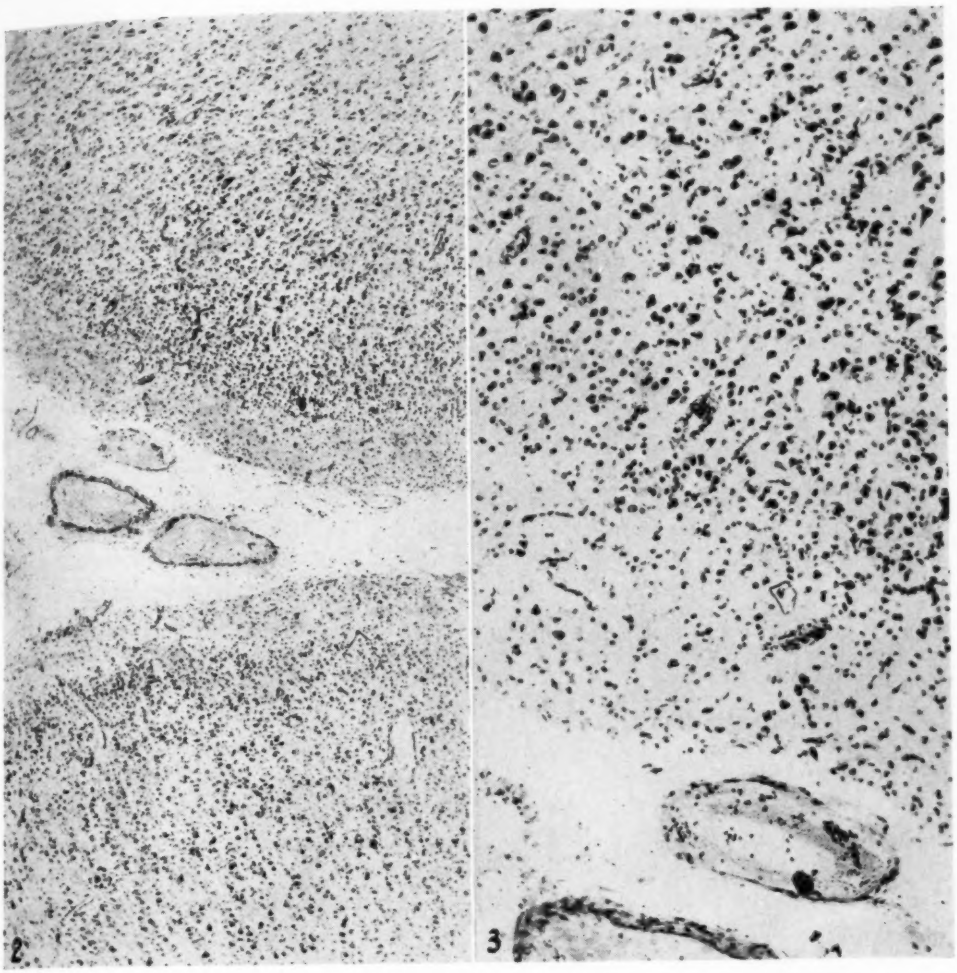

Fig. 2 (Gralnick). Low-power magnification of the cortex to show the rarefaction of nerve cells and consequent disturbed lamination in addition to the increased vascularity and endarteritic changes.

Fig. 3 (Gralnick). High-power magnification of the cortex to illustrate the increased vascularization of various cortical layers.

In the white matter, was found, with various degrees of intensity, a glia proliferation as expressed principally in increase of glia nuclei. Especially surrounding the blood vessels and along the blood vessel walls, were collections and rows of glia nuclei, presumably nuclei of oligodendroglia cells. Fat products of degeneration were found in the various cortical layers in correspondence particularly to the areas where the nerve-cell degeneration was most pronouncd. Fat-degenerative products were found in the perivascular spaces and within the nerve cells.

Concerning the distribution of the pathological findings, it was seen that the frontal, temporal, and occipital areas were more severely damaged than the rest of the brain. In the temporal lobe, it was particularly the Ammon's horn that showed more pronounced vascular and cellular changes. In the Sommer sector of

the Ammon's horn, was found a considerable destruction of nerve cells which at low power gave the impression of discontinuity of the lamina pyramidalis (fig. 4). Fat products of degeneration were more prominent in the Ammon's horn, particularly within the nerve-cell elements. In the cerebellum, vascular changes in the direction of endarteritis were more pronounced in the lamina molecularis. Homogenization of the Purkinje cells was a common finding, and in the white substance glia proliferation of the cerebellum nuclei was quite pronounced. No appreciable clumping of granular cells was noted.

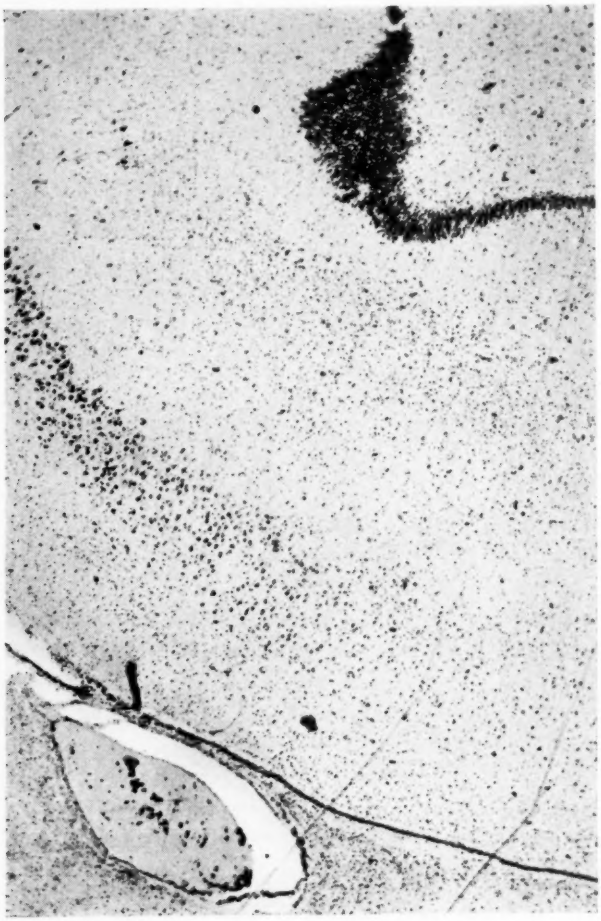

Fig. 4 (Gralnick). Illustrating the disturbance of nerve cells in the lamina pyramidalis of the Ammon's horn.

Comment: Altogether, we were dealing in this case with a diffuse encephalopathy, nonspecific, characterized by two main histopathologic features—involvement of the vascular system and nerve cells. The pathologic findings of the vascular system were along the lines already described in other cases of insulin encephalopathy; that is, hypertrophy and hyperplasia of blood vessels. The endarteritic process was, however, more pronounced here than the proliferative. Both vascular hypertrophy and hyperplasia were present in a moderate degree.

Involvement of the nerve cells consisting mainly of degenerative changes led to a certain amount of destruction of the elements, but not in any pronounced degree. Thus, the cytoarchitecture was affected only here and there, particularly in the frontal, temporal, and occipital areas.

Histopathology of the Eye

The eye was examined by Dr. L. v. Sallmann, of the Department of Ophthalmology, Columbia University College of Physicians and Surgeons. His report follows:

Cornea: The epithelial cover was absent in parts and in others reduced to two or three layers with destruction of normal arrangement. The corneal parenchyma, elastic membranes, and endothelium were normal. Pigment deposits were seen on the posterior surface.

The anterior chamber was normal in depth and content. Filter pectine showed a

great number of pigment deposits. The angle of the anterior chamber was free.

The iris and ciliary body were normal.

Lens: Capsule and epithelium were normal. The nucleus was removed in imbedding.

The *choroid* was normal *in toto.*

The *retina* was artificially detached, in a good state of preservation. The layers were normal in thickness. There were no signs of pathologic changes in the nerve-fiber layer. Ganglion cells (hematoxylin and eosin, Mallory, and different forms of Nissl stain) were mainly normal in number and structure. The nuclei were well preserved with the exception of a few hyperchromatic nuclei lying in an acidophile cytoplasmic mass. Nissl bodies were on the whole unstained (Zenker's fixative). A very small number of them could be demonstrated, lying normally close to the cell periphery in a semicircle. There was no vacuolization of the cytoplasm. The inner and outer granular layers were also well preserved, but a few cells showed pyknotic nuclei with chromatin clumping. Rods and cones seemed to be normal insofar as could be determined in celloidin sections (figs. 5, 6, 7).

The optic nerve showed no lesion in hematoxylin and Weigert sections. Marchi's stain was not applicable because of the fixative.

Diagnosis and Discussion: Abrasion of cornea with regenerative changes of epithelium; scattering of pigment in the anterior chamber; artificial retinal detachment.

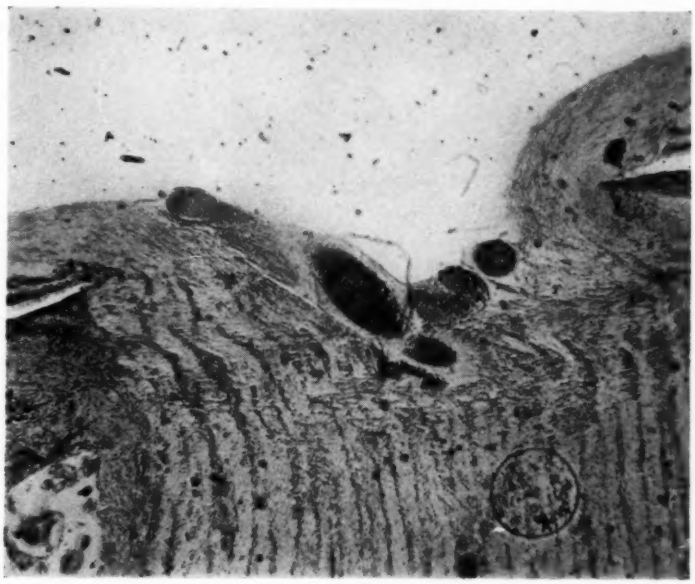

Fig. 5 (Gralnick). Low-power magnification to show normal optic cup with engorgement of the vein. Numerous artifacts above the cup.

The changes of the ganglion cells and the granular layers could not be evaluated on account of the fixative. The pyknotic changes in the granular layers were not extensive enough to be considered pathological but the possibility of a slight degree of degeneration cannot be ruled out.

Summary and Discussion

The literature contains no report on the eye during irreversible insulin coma. Although many brains have been studied,

the retina—which is a similar structure—has not. This paper reports a study of the eye during 10 days of insulin coma. It describes the retina during life and its histopathology in relation to that of the brain after death. It also shows the correlation between the intraocular tension and the blood and spinal pressures on one hand, and the blood- and spinal-sugar levels on the other.

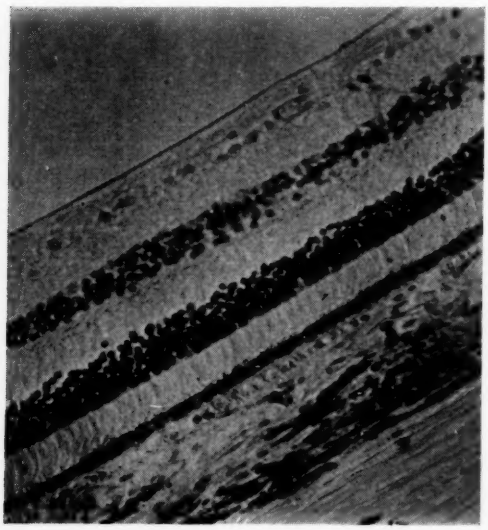

Fig. 6 (Gralnick). Moderately high-power magnification of retina showing normal architecture.

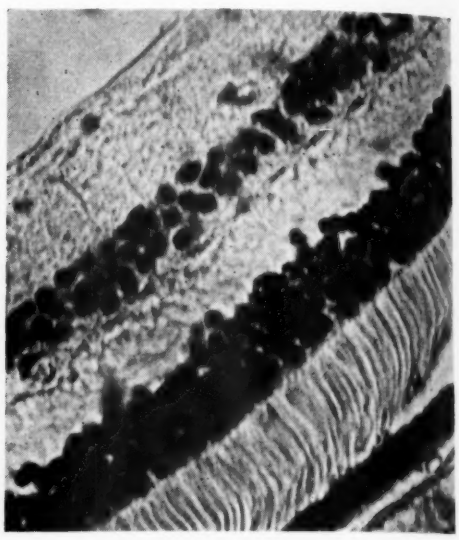

Fig. 7 (Gralnick). High-power magnification of same section of retina showing cellular detail.

The brain pathology will not be discussed here because it has already been covered in comprehensive studies in the literature.[3] It need only be mentioned that in this case the brain changes are typical and extensive.

The retina bears several striking similarities to the brain. Histologically it has a similar cellular structure, and embryologically it is a derivative of the brain. In addition, it too has a respiratory quotient of one, indicating that its chief nourishment is glucose. It could logically be assumed that because of these similarities the pathology in the retina would resemble that in the brain. This, however, does not seem to be the case.

The retinal changes were slight. Those reported here might be due to the coma, but it is just as likely that they were *post mortem* in nature. Certainly with the extensiveness of the brain pathology the retina might be expected to show marked changes. Instead it "was in a good state of preservation," and the ganglion cells, so markedly altered in the brain, were "mainly normal with the exception of a few hyperchromatic nuclei."

Although more similar cases must be studied, we may speculate on the physiological mechanisms proposed to explain the brain pathology,[13] and see if our findings support them. The chief supposition is that insulin hypoglycemia causes an intracellular anoxemia which eventually destroys the brain-cells. Wortis[14] and Himwich[15] state that the brain's diminished metabolism produces the pathology, for in reality there is no anoxemia. The metabolic rate of the retina compares favorably with that of the brain. I do not know, however, how it is affected in irreversible coma of this type. Nonetheless, from the evidence one would expect

a decrease in it also, with resulting damage. It is curious that this did not occur.

A second theory that vascular disturbance produces the brain damage is not well supported by our evidence. The retina showed no focal areas of necrosis, and the vessels were all normal. Even the layer of rods and cones, which has no direct blood supply of its own but gains nourishment from the contiguous choriocapillaris, did not suffer. Perhaps the retina was saved because its blood supply is richer than that of the brain.

If the third concept, that insulin acts as a toxin directly on the brain-cells, is correct, why then does the retina escape? It is very sensitive to other toxins, and should react to insulin if the latter is a damaging agent, and given in large doses.

Himwich[15b] states that the clinical changes occurring in hypoglycemia show that the newer portions of the brain are first affected. Later the functioning of phylogenetically older layers is affected. Heymans[16] says that acute anoxia shows the cerebral cortex most vulnerable, and the upper portion of the brain-stem and medulla less vulnerable in that order. With the aid of electrograms Hoagland[17] showed that during hypoglycemia the activity of the cerebral cortex was depressed before that of the hypothalamus.

From the foregoing Himwich[15b] supposes that the older portions of the brain are less sensitive. They have smaller energy requirements, and are therefore more resistant to hypoglycemia than younger parts with their higher metabolic rate. Thus, when sugar is given, the older parts are first to recover. All of this may account for the phylogenetically older retina's apparent resistance to damage during coma. In addition the blood-sugar level of this patient could have been high enough to spare the retina but not the brain. The disconcerting feature, however, is that studies[7, 8, 9, 11] show the retina's metabolic rate to be very high. It should thus be responsive to hypoglycemic changes despite its older phylogenetic age.

The intraocular tension in the case presented was uniformly low, declining to very low levels in the last days of life. This finding agrees with that of many who have made a similar observation during routine insulin comas.[18] The ocular tension showed no correlation with the blood pressure or of the sugar levels of the blood and spinal fluid, but did fluctuate somewhat inexactly with the spinal pressure.

The spinal-fluid pressure was uniformly low. This fact, coupled with the diminished amount of fluid in the ventricles and the failure to obtain a spinal pressure during the last three days, despite cerebral edema, may account for the lowered intraocular tension. Obviously, there was some defect in the system that forms spinal fluid and maintains its pressure. Perhaps this was in the choroid plexus, for the blood pressure stayed at a good level.

Ophthalmoscopic examination of the retina was normal during life, and confirmed by the microscope. This evidence supports my previous finding[1] that insulin coma, routinely given, does not affect the retina.

Conclusions

In prolonged insulin coma of 10 days' duration: (1) The retina appeared to escape damage although the brain sustained extensive injury. (2) The ophthalmoscope revealed no gross pathology. This finding supports one made in a previous paper that the fundi are negative in patient with functional psychoses given routine insulin-shock therapy. (3) The intraocular tension remained uniformly low, and fluctuated inexactly with the spinal pressure. (4) The intraocular tension had no relation to the blood pressure or blood- and spinal-sugar levels. (5) The finding of lowered intraocular tension corresponds to that of most investigators who

report the same in routine insulin comas of short duration.

The writer wishes to express his thanks to Dr. Marcus Shatner of Central Islip State Hospital for his coöperation, and to Dr. E. Burchell of the New York Eye and Ear Hospital for preparation of some of the slides studied.

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OCULAR ONCHOCERCIASIS*

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American onchocerciasis was discovered in 1915 by Dr. Rudolfo Robles, a physician in Guatemala. In America this disease has been observed only in Mexico and in Guatemala. In the latter country it has been studied by Robles, Calderón, Pacheco Luna, Estevez, Diaz, Strong, Mira, and de Leon; in Mexico, by Ochoterena, Hoffmann, Toroella, Silva, Larambe, and some others.

Onchocerciasis as it exists in Africa is caused by Onchocerca volvulus; it has various appearances, and in many of its manifestations is identical with American onchocerciasis. The changes in the eye in African onchocerciasis have been described by Hissette.

In Guatemala the disease is limited to three zones, which are found at an elevation of 1,200 to 4,500 feet above sea level.

Before giving a description of ocular onchocerciasis, I shall present a résumé of generalized onchocerciasis.

AMERICAN ONCHOCERCIASIS

The onchocerca in man is manifested by the presence of fibrotic nodules localized more or less superficially. They are found with more frequency under the hairy skin, along the ribs or crest of the ilium, near the elbow, and as a general rule near the flat bones. These fibrotic nodules contain the adult parasite, a species of the genus onchocerca, Onchocerca caecutiens.

The female is a filiform worm which measures 30 to 50 cm. in length. The male measures 2 to 3 cm. in length and is 0.2 mm. thick. One or several females or males may be found in a tumor. The fecund female contains thousands of eggs, some already embryonic, and many embryos or microfilaria that move actively. When liberated from the mother, these microfilaria emerge from the nodule, erupting through the skin, and spreading all over the surface of the body. They measure 300 to 400 micra in length and 10 to 15 in thickness.

A biopsy of the skin of an individual infected with filaria, shows living microfilariae, and in general the nearer the biopsy is made to the tumor, the greater the number of microfilariae found.

Skin changes are produced when the microfilariae are very abundant. When the process resembles erysipelas, there is a thickening and hardening of the skin of

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the face which give the patient a characteristic appearance. The tumors are tolerated without much trouble, and never induce inflammatory reaction. It may be said that outside of the erysipeloid form, which is seen but rarely, the only damage that onchocerciasis effects is manifested in the vision. It is for this reason that onchocerciasis should be considered as a disease of the eyes.

Transmission is by Simulium flies as intermediaries. Robles of Guatemala, when describing onchocerciasis, suggested that the Simulium fly could be the vector of the disease, which was confirmed later.

The fly bites an individual and imbibes many microfilariae. Within the fly, the microfilaria follows part of its evolutionary cycle. At first, its movements appear to be excited and are made violently. Later the parasite begins to grow. It is thought that 8 to 10 days are needed for the parasite to attain the stage called infective; that is to say, ready to be transmitted to man.

The early extirpation of the nodules, or source of microfilaria, is preventive treatment for the ocular lesion. Although it is not definitely known how long they live, the microfilariae disappear in 4 or 5 months after removal of the tumor. The serious problem is presented when the microfilariae are in the skin and eyes and cannot be localized in a nodule. Various treatments have been tried to destroy the microfilaria, but there is no effective remedy as yet.

Ocular onchocerciasis

The ocular changes of onchocerciasis are produced by the presence of microfilaria in the eye. I used to think that the "toxins" that the adult parasite produced in the nodule were responsible for the ocular signs; however, I have never found ocular changes without having been able to prove the presence of the microfilaria in the eye, in one form or other.

The ocular symptoms appear fairly soon after the formation of the nodule. The course of the ocular affection is insidious. At first irritation and congestion, lacrimation, and photophobia are the most important symptoms. Sunlight and artificial light even though not excessive disturb the patient a great deal. There are also slight changes in the accommodation, and fatigue.

This period of the onset can last a long time; if the influence of the microfilaria on the eye is slight, many years. When there are several nodules, and especially if they are located in the head, the course of the ocular affection is more rapid. The photophobia increases, and the signs of a subacute iritis are observed. Sometimes there is a period of quiescence, as if there were an adaptation, only to have the picture of iritis repeated: ciliary congestion, slight turbidity of the aqueous humor, small and only slightly mobile pupil, and in serious cases posterior synechiae, pupillary membrane, and occlusion of the pupil.

The *advanced* lesions of onchocerciasis may be divided into three types: (1) that in which the principal lesion is anterior or the inflammation subacute, in which the cornea, iris, pupil, and ciliary body are especially affected; (2) the type with posterior localization with only a slightly appreciable inflammatory reaction, including changes in the choroid, retina, and optic nerve (there are severe cases of this type in which only close examination can show us alterations of the anterior segment of the eye); (3) a combination of the first two types, complicated sometimes by secondary glaucoma. The three types frequently lead to blindness.

Fortunately, in the great majority of cases of onchocerciasis, only benign ocular symptoms, or those of the onset, are observed.

Examination of an individual with symptoms of the onset shows us slight

changes of the conjunctiva: congestion, a little filamentous secretion, and lacrimation. If a biopsy specimen of the conjunctiva is taken and the tissue is placed in physiological salt solution under the microscope, in a few minutes one can see the microfilaria emerging with active movements.

The cornea shows the keratitis characteristic of onchocerciasis. There are small whitish opacities near the limbus in the horizontal meridian, both on the nasal and temporal sides; they are round and about 0.25 to 0.5 mm. in diameter. Almost always they are multiple, and on rare occasions appear conglomerate in the beginning. In general, they are located in the most superficial part of the substantia propia of the cornea, but it is not unusual to see them deeper in the tissue. They are the result of the inflammatory reaction produced by the body of a dead microfilaria in the cornea. With the slitlamp I have been able to follow the behavior and evolution of the microfilaria in the cornea. Between the fibers of the substantia propria of the cornea, the larva remains almost immobile, and it may be seen to elongate to effect its characteristic movements. Although very slowly, it changes its position on rare occasion, retraces its progress, and disappears from the cornea.

Generally, perhaps from its imprisonment in the hard substance of the cornea and from not having found sufficient nutrition, it dies in the cornea. Then commences its disintegration and the inflammatory reaction which this produces. At the two ends one can see that the sharpness of demarcation is lost and there is formed a zone of opacity around the extremities; later the rest of the body also disintegrates, and by the juncture of the two opacities that have been formed at the ends, a large opacity of circular form occurs. This is the origin of what is called "punctate keratitis" of onchocerciasis. These opacities may become very numerous. They are most numerous at the periphery near the midline of the cornea.

Another of the changes in the cornea, which although not constant is observed frequently, is a collection of coffee-colored pigment, also localized in the horizontal meridian on both sides, very near the limbus. With the slitlamp it is observed to lie superficially in the substantia propria, and to be composed of thousands of tiny patches of pigment. These particles have an elongated form and resemble groups of bacilli, all oriented in more or less the same direction. Although the microfilaria disappears for one reason or another, the pigment remains in the cornea for a long time. It seems to be a continuation of the process of pigmentation that is observed in the conjunctiva when the onchocerciasis has remained for some time, and that is also localized along the temporal or nasal side, near the cornea.

Vascularization is another of the lesions of the cornea caused by the onchocerca. It may be superficial or deep. Generally it is observed in old advanced cases, when the transparency of the cornea is affected; and above all when in the progress of disintegration of the dead microfilariae, phenomena of reaction with exudation that have produced changes in the epithelium of the cornea have taken place. This vascular reaction greatly resembles the "pannus" of trachoma, but its localization is on the nasal and temporal sides and slightly below; almost never is there superficial vascularization above.

Deep vascularization is observed also in cases of old corneal lesions. It is rather moderate and very similar to interstitial keratitis. There can be no doubt that the origin of this vascularization is for defense, to aid in the absorption of the remnants of the microfilariae and their toxins, and to supply the deficient nutrition of a cornea with many points of

altered transparency. In cases in which the influence of the microfilaria is not excessive, I have seen these states of vascularization favorably modified by treatment with compounds of riboflavin.

Changes in Descemet's membrane caused by onchocerciasis cause its loss of transparency. Small areas of exudate are seen frequently on examination with the slitlamp, and on careful observation one can see vertical folds in the membrane. On the endothelium of the cornea are deposited particles of pigment from the iris, but only in slight amount. Whitish deposits of leukocytes on the endothelium are rare; when they do occur they are very scanty.

Lesions induced by onchocerciasis do not effect changes in the sensitivity of the cornea, and only in the cases in which the epithelium has been seriously disorganized is there diminution of the sensitivity and staining of parts with fluorescein.

The anterior chamber will present the picture of subacute plastic iritis. In advanced cases with pronounced iris lesions the angle of the anterior chamber loses its depth, especially below. Almost in all cases of ocular onchocerciasis, even at the onset and when the symptoms are but slight, one can see the microfilariae free in the anterior chamber; they float, moving very actively, and with retroillumination by the slitlamp they can be followed for a long time, and occasionally are seen to disappear behind the iris. As they are not numerous in the anterior chamber, examination must be made with great minuteness if one wishes to find them. Many times I have found them only after four or five examinations on different days in individuals in whom the onset of ocular participation of the disease was only suspected.

The changes of the iris and the pupil are characteristic; and it is not difficult to make a diagnosis of onchocerciasis when these lesions acquire their typical aspect. During the early stages the iris presents the aspect of subacute iritis; later it begins to swell, especially towards the pupillary border.

The pupil acquires in some cases the appearance of "the hole in a doughnut." The pigment border, the continuation of the pigment layer of the iris, disappears in the inferior segment, and at times completely; the iris swells up increasingly near the pupil; the latter loses its mobility and becomes elongated vertically below. Later, posterior synechiae are formed, and the exudation may lead to occlusion of the pupil. In this condition the pupil appears to be irregular and very small. After the period of swelling of the iris and if the disease has tendencies to advance, the onset of atrophy of the iris supervenes, with patches in which the iris has lost its normal color and becomes thinned.

During this period, the vascularization of the iris, which is visible in some cases, increases and often comes to cross the pupil. I have seen cases of almost complete atrophy of the iris.

In other advanced cases there is no pupillary occlusion, but rather an exaggerated lengthening downward, which gives the impression that an iridectomy has been made.

With the slitlamp one cannot see the microfilariae in the iris, but I have had occasion to see them coming out from this layer with only part of their forms free. By patiently observing these cases one can see them liberate themselves completely. In histologic sections one can appreciate very well their growth, and segments of microfilaria are seen in the muscular layer of the iris. The irritation produced by the larvae and their toxins in an iris already sensitive and irritated seems to me one of the causes of the photophobia so constantly observed in cases

of ocular onchocerciasis.

The lens does not suffer very great modifications when the disease takes a benign course, apart from some depositions of particles of pigment from the iris which adhere to the anterior capsule. In advanced cases and when there has been considerable inflammatory reaction, opacities and complete opacification of the lens are frequently manifest.

During the course of inflammatory alterations of the anterior segment of the eye, constituting the first group mentioned, the ocular tension is maintained at normal or subnormal; but it is frequent to observe cases complicated by secondary glaucoma, and in these cataracts are developed peculiar to this affection. It is to be noted that the iridocyclitis of onchocerciasis with secondary glaucoma is particularly refractive to treatment.

The lesions of the fundus of the eye, which can be observed when there is slight involvement of the anterior segment, are atrophy of the optic nerve and chorioretinitis of various types.

Atrophy of the nerve is observed in young individuals who have suffered from onchocerciasis with multiple tumors of the head or adjacent regions. I have never observed atrophy without other ocular symptoms, and above all without other lesions in the fundus. The course followed is slow; there is a progressive contraction of the fields of vision and central vision decreases gradually.

In the cases in which there are increases in the intraocular pressure, and this is continued for some time, the nerve presents a typical glaucomatous excavation, and the fields of vision suffer the changes typical of glaucoma.

Chorioretinitis is the rule when the ocular lesion has been active for a long time. Rarely does it develop acutely; usually its course is very slow. There are deposits of pigment, which, without other visible signs, accumulate in the neighborhood of the nerve. At first there appear blackish areas which unite to form thicker patches. These changes also occur in the rest of the fundus, and the macula is often affected. It is not unusual to see large masses of black pigment near a white area of bared sclera.

There is another type of retinitis that is observed, especially in old cases, in which the anterior segment has been slightly affected; this is the type that resembles retinitis pigmentosa, with its appearance of "salt and pepper" in the retina, especially in the periphery. The arteries are very much diminished in caliber; there are zones of exudation along the vessels. These patients complain of difficulty in seeing at night. Outside of very limited cases and others in which the data cannot be obtained with certainty, one can be sure that no familial nor hereditary factor exists in the patients of this type which could make one think of an etiology other than onchocerciasis.

Summary

American onchocerciasis should be considered as an ocular affection. Only complications in the eyes are serious.

The nodules ought to be excised. When cases of onchocerciasis present themselves without apparent tumors, these should be searched for with great care.

Treatment to destroy the microfilaria will avert ocular complication. Such treatment is still to be discovered.

NOTES, CASES, INSTRUMENTS

A PORTABLE SLITLAMP*

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The slitlamp has become an essential piece of equipment for the ophthalmologist, and the younger ophthalmologists are far more dependent upon it for diagnosis of external ocular conditions than were their predecessors. Satisfactory examination of a patient in the home or hospital is often impossible without the use of slitlamp microscopy.

The writers believe they have designed a portable instrument that retains most of the features of the major slitlamps but that can be used in the home, hospital, or office, and one that can be purchased for less than half the price of the larger instruments.

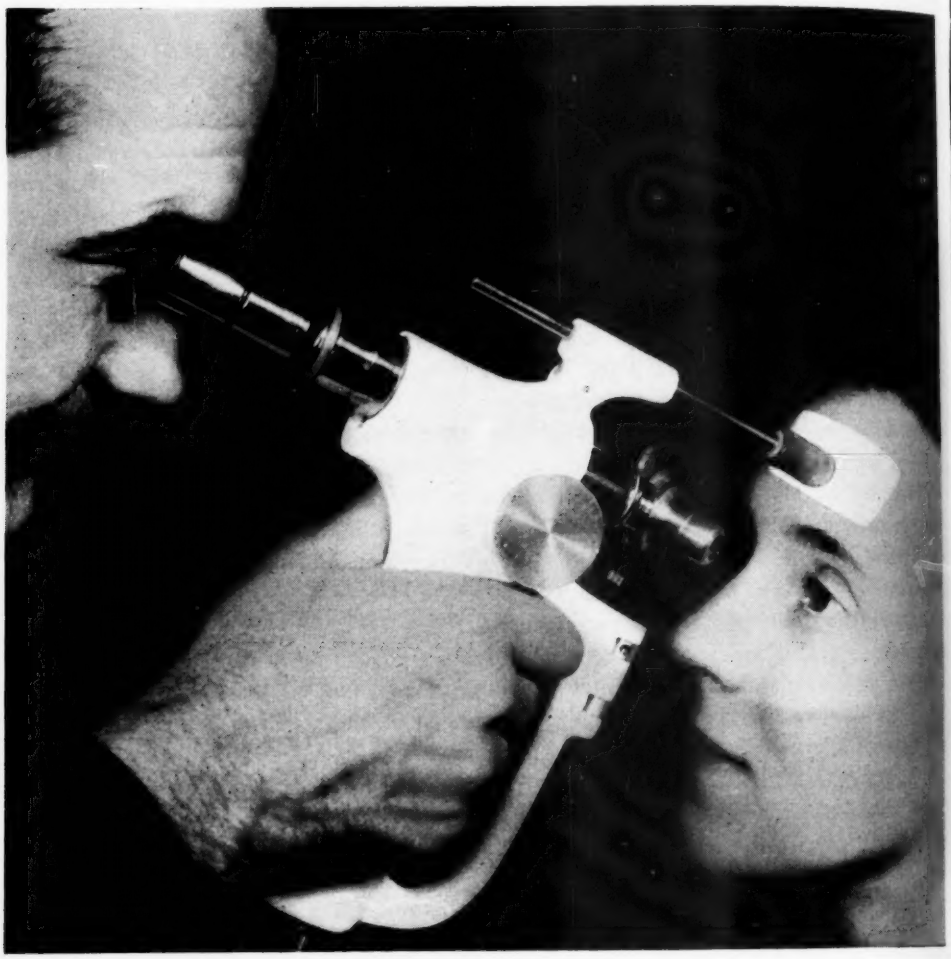

Fig. 1 (Bettman and McNair). The slitlamp in use as a hand instrument.

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It is pertinent to consider some of the essential principles upon which adequate slitlamp technique is dependent:

The great advantage of slitlamp microscopy over examination with ordinary oblique illumination is the fact that an optical section can be examined. A well-defined optical section depends upon brilliant illumination and accurate focusing of the image of the slit.

If the lamp arm does not move absolutely independently of the microscope, much of the advantage gained from a brilliant narrow optical section is lost.

The apparatus must permit firm contact with the patient's head; otherwise adequate focusing is impossible.

The microscope should, likewise, permit adequate focusing. Although the designers of the larger slitlamps have all taken cognizance of these principles, they have constructed instruments without regard for size, portability, or expense.

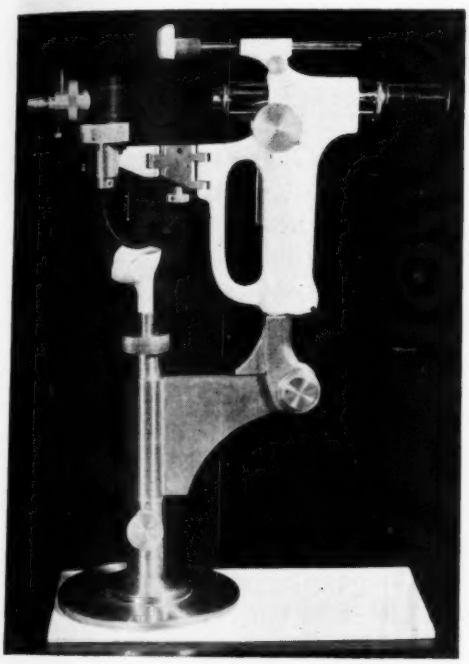

Fig. 2 (Bettman and McNair). The slitlamp mounted on a stand for use at the refractionist's table.

The instrument presented in this paper represents an attempt to construct a portable and relatively inexpensive slitlamp that embodies the features essential to good biomicroscopy.

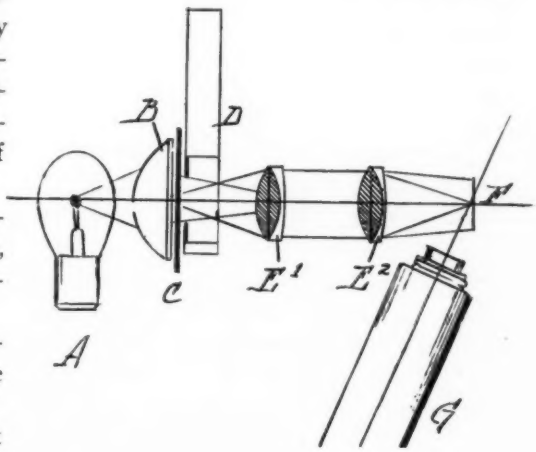

Fig. 3 (Bettman and McNair). Schematic drawing of the lamp and condensing lens system.

As may be seen in the accompanying photographs, the instrument may be used in the hand (fig. 1) or supported on a small stand (fig. 2). The magnification is supplied by an ordinary monocular microscope with an erecting system. A 10× ocular and a 48-mm. objective are used. Magnification may be varied from 8 to 25 diameters by altering the length of the tube. The microscope is focused on a rack and pinion with a wheel on either side of the instrument that can be operated by the thumb of either the right or left hand—depending upon which eye is being examined.

The lamp and condensing lens system are shown diagrammatically in figure 3. The lamp contains a special rectangular-shaped filament that is present only in the center of the lamp and thus produces a concentrated spot of light. It operates on

a 7-volt transformer with a 3-ampere output. The condensing system supplies an exceedingly narrow brilliantly illuminated slit that can be accurately focused. The width of the slit can be varied at will. The length can be altered from a bundle of light 0.5 mm. in diameter to a slit 5.5 mm. long.

The lamp and condensing system are supported by an arm that can be moved without moving the microscope. Thus, illumination can be directed toward the eye at any desired angle, and can be used from either the right or the left side of the microscope. When the arm is in the desired position it can be locked. A small knob on the illuminating lens permits accurate focusing of the light at the desired depth in the eye, as in any of the large slitlamps.

The headrest is an essential part of the instrument. It is pressed firmly against the patient's forehead, the patient's head being braced against the back of a chair, or against the pillow if he is in bed. The slitlamp is steady but can easily be moved in any direction by sliding the rest along the patient's forehead.*

The value of a monocular microscope may be questioned by some. The judgment of depth depends far more upon focusing along the optical section than upon stereopsis. A binocular microscope would increase the cost and weight of the slitlamp to a degree that would outweigh any advantages obtained.

It is not within the scope of this paper to enumerate the many conditions in which the slitlamp is of aid as a diagnostic instrument. Thep ortable slitlamp is primarily intended for the examination of nonambulatory patients in whom it is important to determine the depth of a penetrating wound, presence of injury to the lens capsule, or of an aqueous flare, and the like. The instrument may also be used at the refractionist's table to make routine biomicroscopy more convenient.

450 Sutter Building.

* Although somewhat unwieldy, the instrument is not unduly so—as is the case with any new instrument, a moderate amount of practice is necessary to become adept in its use. It is not as unsteady as one might think if the patient's head is pressed firmly against the back of the chair or pillow, and the rest on the instrument is pressed securely against the patient's forehead. I have used it repeatedly in examining rabbits' eyes and have found it easy and more convenient than larger instruments. It is manufactured by Wood-McNair, Instrument Makers, 12 Geary Street, San Francisco, California.

BLACK AND WHITE SILK SUTURES*†

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Because of the greater danger of infection when catgut is used and the marked reaction observed following resection,[1] retroplacement,[2] and transplantation of Tenon's capsule[3] for adhesions between the sclera and the ocular muscles, unusually fine silk sutures have been developed.† These sutures have produced little reaction and the white silk sutures are especially valuable when it is desirable to bury sutures, as in the operations mentioned above. The double-armed black silk sutures have been developed especially for keratoplasty but are useful in conjunctivoplasty, transplantation of pterygia, and muscle operations when the sutures are brought through the conjunctiva and tied on plastic strips or buttons.‡ The single-armed black silk sutures were designed especially for suturing cataract wounds.[4]

Description of white silk sutures. These unbleached sutures (designated P290) consist of pure silk, free from the

* Made by Davis and Geck, Brooklyn, New York.

† Development aided by the Ophthalmological Foundation, Inc.

‡ Made by V. Mueller and Company.

natural gum. The silk is size six-0, this gauge having been determined on a standard micrometer. Each suture is 12 inches in length and double-armed with delicate three-eighths-circle atraumatic needles with cutting point.

Description of black silk sutures. These sutures consist of Anacap black silk that is specially treated to render it absolutely noncapillary under all conditions to which sutures are exposed. In addition, this material is nonirritating to the tissues, and it ties readily into a firm knot that does not slip. It retains all the smoothness and flexibility of natural untreated silk, yet new principles of fabrication make it handle more easily and tie more securely. Moreover, it is unaffected by boiling or autoclaving or by the action of tissue fluids, antiseptics, or irrigating solutions.

The sutures are 12 inches in length and either single-armed (P276) with one delicate three-eighths-circle atraumatic needle with cutting point, or double-armed (P277) with two delicate three-eighths-circle atraumatic needles with cutting point.

35 East Seventieth Street.

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[2] ——, Losey, R. R., and Connolly, P. T. Retroplacement for strabismus. Amer. Jour. Ophth., 1929, v. 12, Sept., p. 720.

[3] Berens, C. Tenon's capsule transplants in surgery of the ocular muscles, with especial reference to postoperative deviations with adhesions between the muscles and the eyeball. Amer. Jour. Ophth., 1938, v. 21, p. 536.

[4] ——, and Losey, R. R. An untied conjunctival suture and conjunctival bridge in cataract extraction. Results and conclusions. Brit. Jour. Ophth., 1936, v. 10, p. 576.

SOCIETY PROCEEDINGS

Edited by Dr. Ralph H. Miller

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

April 1, 1940

Dr. Mark J. Schoenberg, *chairman*

The April meeting of the New York Society for Clinical Ophthalmology was devoted to a discussion of glaucoma.

Realizing the complexity of the subject and the many divergent views concerning nearly every phase of the disease, it was deemed advisable to deviate from the conventional methods of presentation and to adopt the method of round-table discussion which has found such popular acceptance in connection with sociological problems.

This program was in the nature of an experiment, and as such lends itself to many modifications and improvements. The method also may be varied as the nature of the subject or of the audience requires it. However, even in its present form, it met with enthusiastic approval of the vast majority of those present at the meeting, which incidentally drew a record attendance.

The method represents a radical departure from the usual reading of papers and formal discussion. Its success and general appeal has encouraged us to bring it to the attention of the readers in the hope that others may want to try it out.

Careful planning and preparation of the program is of prime importance to assure success to such a meeting. The procedure followed is therefore being reported in great detail.

Last December the program committee put Dr. Mark J. Schoenberg in charge of organizing the program. Over three months were spent in its preparation. The first step was to urge all members through letters and personal contact to submit questions and problems pertaining to glaucoma. About 100 questions were received. These were classified under the various headings, such as diagnosis, pathogenesis, and treatment.

A panel of five outstanding men, who are interested in the subject and whose opinions are respected, was then chosen. Each of these men selected three questions which he desired to discuss or answer, each answer not to exceed five minutes. The answers were in turn discussed by the other members of the panel, two minutes being allowed for each discussion. The member in charge of the program acted as the chairman of the panel. He introduced the questions and took part in the discussions.

The second part of the program consisted in a discussion from the floor. Selected members of the audience were invited to ask questions of any member of the panel, or to make brief remarks.

The main features of this method of discussion are:

1. The questions chosen are those which the members of the society themselves have asked.
2. The questions are answered by men qualified to express their opinions and, furthermore, each man chose those questions which fall in line with his own experience and special knowledge.
3. The audience is given an opportunity to take part in the discussion and to have certain answers clarified.

It is not claimed, of course, that this method is suitable for the presentation of original communications, but in a discussion of a complex subject it offers the advantage of permitting many phases to

be covered within the scope of a single meeting.

The members of the panel were: Drs. John Evans, Jonas Friedenwald, Joseph Igersheimer, Arnold Knapp, Ervin Török, and Mark J. Schoenberg, chairman.

QUESTION I: WHAT IS YOUR DEFINITION OF GLAUCOMA?

DR. EVANS: It is impossible to give a definition of glaucoma. One can only outline the phases for discussion. For temporary use we might say that primary glaucoma is a heterogeneous entity characterized by vascular crises and accumulation of fluid within the eye. It is ultimately associated with increased intraocular pressure, optic atrophy, ganglion-cell death, and the formation of synechia in the angle of the anterior chamber.

DR. SCHOENBERG: Do the members of this group agree with Dr. Evans's definition?

Since no one wishes to discuss the subject, I should like to ask Dr. Evans whether his definition includes the so-called "secondary glaucoma"? Is there such a thing as "secondary glaucoma"?

DR. EVANS: Your question embraces all of medicine.

DR. SCHOENBERG: I believe that the term "secondary glaucoma" is a misnomer. "Secondary glaucoma" is not glaucoma. The fact that the ocular tension is often elevated in iridocyclitis should not mislead us into calling this condition glaucoma. The conception that ocular hypertension is glaucoma and glaucoma is ocular hypertension ought to be given up. The average ophthalmologist is inclined to treat any ocular hypertension with pilocarpine and eserine—the higher the hypertension, the stronger the solution. Well, many of the cases of iridocyclitis with hypertension not only fail to respond to these miotics but react by still higher tension and more marked congestion.

The failure to recognize the contraindication of miotics in this type of iridocyclitis is due to the traditional acceptance of the term "secondary glaucoma." Ocular hypertension, accompanying iridocyclitis, retinal thrombo-phlebitis, intraocular tumors, and the like, is certainly not glaucoma. Why call it "secondary glaucoma"?

DR. TÖRÖK: I would eliminate the term "primary glaucoma." It is not a disease; it is a symptom of the eye. Primary glaucoma presents a condition in which the disease cannot be discovered. But the disease is there. Secondary glaucoma is not a glaucoma; it is an iridocyclitis. Or it is a trauma, but it is not glaucoma.

DR. SCHOENBERG: Dr. Igersheimer, what is your opinion?

DR. IGERSHEIMER: I do not see any other way out. Ocular hypertension and the excavation of the optic nerve are two definite signs we have to keep in view when we make a diagnosis of glaucoma. But in some cases, we find no hypertension, only a glaucomatous excavation. Would you call that glaucoma?

DR. KNAPP: The term "secondary glaucoma" is well chosen. It simply means that you have a case of hemorrhages or something else in which there is a very definite complication; namely, a complication of increased tension which should be promptly attended to.

QUESTION II: WHAT IS MALIGNANT GLAUCOMA? COULD IT BE RECOGNIZED BEFORE THE OPERATION?

DR. KNAPP: To my mind malignant glaucoma consists in the nonrestoration of the anterior chamber after operation for glaucoma. The condition seems to me to be rather an expression of a paretic condition of the suspensory apparatus of the lens and this part of the eye becomes stretched.

Can it be recognized before operation? It can be frequently recognized before as the eye presents an extremely shallow anterior chamber.

DR. TÖRÖK: I do not think one can diagnose a case of malignant glaucoma preoperatively. We find, however, that at times following iridectomy, trephining, or Lagrange operation the anterior chamber does not re-form, the lens is pushed forward, and the tension increases. The increased tension cannot be relieved and finally the eye becomes blind. In other words the eye develops what is called malignant glaucoma. This condition is more apt to develop in cases of simple glaucoma and therefore in these cases no operation should be performed in which the anterior chamber is opened and the aqueous is evacuated. In simple glaucoma, therefore, the operation of choice is cyclodialysis, as in this operation, if it is performed properly, the aqueous is not lost.

DR. SCHOENBERG: Dr. Igersheimer, what is your experience with cases of malignant glaucoma? Could you make a diagnosis before operation?

DR. IGERSHEIMER: Only in cases with disease of the vessels of the iris which we see with the slitlamp. I think sometimes we have cases in which there is marked disease of the vessels and in these I think it is possible to predict a malignant glaucoma.

DR. SCHOENBERG: There are cases of malignant glaucoma which do not belong to the group with diseases of blood vessels of the iris. These cases do not respond to miotics and react disastrously to iridectomy or trephining. Could the malignancy be recognized before the operation? The patients I have seen were between 35 and 40 years of age. The anterior chamber, and especially the angle, are extremely shallow. It would be very important to know why the anterior chamber is so shallow. Does the swelling of the vitreous and of the ciliary processes play the main role in bringing about this condition? But why should the vitreous or ciliary body and processes swell? Why should the condition become aggravated by an iridectomy or Elliot operation? The entire picture reminds one of an allergic reaction of the tissues to a "foreign" protein or to operative trauma.

DR. TÖRÖK: But how are you going to know if the eye is allergic?

DR. SCHOENBERG: I believe that the early occurrence in life (35 to 40 years of age), the very shallow angle of the anterior chamber, the lack of response to miotics, a history of allergy in other parts of the body and, above all, the history of an unfavorable reaction to surgical trauma in the first eye are helpful points in making the diagnosis of malignant glaucoma in the second eye.

DR. TÖRÖK: I would not perform an operation in a case of glaucoma in which there is no rise of tension but only excavation.

DR. KNAPP: My experience in cases of malignant glaucoma is a little different. Dr. Igersheimer's statement that you can predict a malignant glaucoma on account of vascularization of the iris I do not think is quite true, because that again is a different pathological condition. We naturally hesitate to operate in cases in which there is a suspicion that they may become malignant.

QUESTION III: WHAT IS THE CAUSE OF OPTIC ATROPHY CONTINUING TO PROGRESS AFTER A SATISFACTORY DECOMPRESSION OPERATION IN A GLAUCOMATOUS EYE?

DR. IGERSHEIMER: There are two degenerative processes in the optic nerve in glaucomatous eyes. First, an ascending atrophy due to the degeneration of the inner layer of the retina and of the

nerve fibers in the papilla. This degeneration is the consequence of the ocular hypertension. The second atrophic process is in Schnabel's caverns in front of or behind the lamina cribrosa, restricted to the vascular part of the nerve. Many authors believe that this cavernous process has a relation to the ocular hypertension too, in such a way that the hypertension disturbs the circulation in the small vessels of the lamina cribrosa and its surroundings. The conception that the caverns are a product of circulatory disturbances has not been absolutely proved as yet. If this were true, then one could understand that a disease of these small vessels—also without ocular hypertension—might produce caverns and the process might continue even after a satisfactory decompression operation. It also was pointed out that there are sometimes retrobulbar degenerative processes, which have not a real cavernous character. I want to show you some lantern slides of an interesting case.

A 42-year-old patient with chronic glomerulonephritis, general hypertension, and uremia was, in the course of one-and-one-half years, admitted four times to the medical department of Professor Volhard in Frankfurt. Each time he was examined in the eye clinic as well. The first two times (July 23, 1929, and July 23, 1930) a physiologic excavation was found, but the last two times (November 18, 1930, and February 7, 1931) the excavation had a real glaucomatous character with overhanging margins. Sections through the optic nerves of both eyes showed areas of atrophy; on the right side directly behind the lamina, on the left side several millimeters behind the lamina. This degenerative process could not be found farther back in the orbital portion of the optic nerves. Besides this degeneration there were also small caverns. Such other signs of ocular hypertension as iris-root synechiae could not be found anatomically. It is, of course, very probable that in this patient, with secondary contracted kidney and certain vascular changes in several parts of the body, the disease of the optic nerve was due to circulatory disturbances. But I must admit that I could not prove this.

DR. KNAPP: It is important to realize that there exists an optic atrophy with cupping which is not due to increased tension. I should like to ask Dr. Igersheimer: Can Schnabel's caverns be due to disease in the smaller vessels of the optic nerve?

DR. IGERSHEIMER: Microscopic studies have not yet cleared up this question. There are authors like Morax who point out that vascular disease was the only explanation for the development of Schnabel's caverns, but real proof for this conception does not yet exist.

DR. SCHOENBERG: Is there any remedy that could arrest the progress of the optic atrophy after the ocular hypertension has been eliminated by a successful operation?

DR. IGERSHEIMER: I do not know any remedy for such an atrophic process.

QUESTION IV: HOW WOULD YOU HANDLE A GLAUCOMA PATIENT'S ONLY EYE WITH A GOOD FILTERING SCAR AND CATARACT?

DR. TÖRÖK: Operation in these cases does not differ from the usual cataract operation except that the incision should not be carried through the filtering scar but should end anterior to it in the cornea. Since such a wound does not gape easily the incision should be made a little larger than usual.

DR. KNAPP: I would add the desirability of extracting the cataract in the capsule. If the capsule remains, there is interference with healing after the operation.

DR. IGERSHEIMER: I would attempt an intracapsular extraction through the old

scar. I saw an eye which was operated upon through the scar and it healed very well.

QUESTION V: OUTLINE A ROUTINE TREATMENT OF ACUTE GLAUCOMA IN A PATIENT SEEN WITHIN 24 TO 36 HOURS AFTER ONSET

DR. KNAPP: We have adopted the following procedure: The patient is put to bed; Elschnig's triple drops (pilocarpine, eserine, and cocaine) are instilled every 15 minutes; an artificial leech is applied to the temple; ice compresses; the patient is given a hypodermic of morphine. Usually this reduces the tension. In any case it is better to wait 24 hours before performing the operation. In some cases after a number of days the tension goes up again so that I have made it a rule not to wait, but to perform an iridectomy.

DR. TÖRÖK: I would give the patient in addition a good strong physic. I do not like artificial leeches. I prefer natural ones.

DR. IGERSHEIMER: General treatment is essential too. It is well in the first two days to give some intravenous injections of sodium chloride or sugar.

DR. EVANS: I use the same routine.

DR. KNAPP: If, after the second day, the tension does not come down it is best to operate; after retrobulbar injection the tension often comes down and permits an iridectomy. If, however, that does not take place, a posterior sclerotomy should first be done.

DR. SCHOENBERG: A few more minor details deserve, perhaps, to be mentioned. The patient should not be kept in a semi-dark room; he should have at least two pillows underneath his head, friends and relations should not be allowed to visit, especially if they have a cough or a head cold, or if they are apt to upset the patient's peace of mind.

QUESTION VI: GIVE OPERATION OF CHOICE IN HYDROPHTHALMOS AND JUVENILE GLAUCOMA

DR. TÖRÖK: Operations in cases of hydrophthalmos are usually accompanied by severe complications such as prolapse of vitreous, dislocation of lens, detachment of retina, and the like. Operative interference should be resorted to only when absolutely necessary, and then my operation of choice is cyclodialysis.

There is no difference between juvenile and senile glaucoma except the patient's age. The indications for operation are therefore the same in both instances.

DR. IGERSHEIMER: My experience has not been very good in these cases. I have generally also performed a cyclodialysis, and it is really much better than a trephining. But several times following a cyclodialysis in such cases I saw severe hemorrhages with unpleasant consequences. But there are some cases in which I think the prognosis is not very bad, if operation does not take place too late.

DR. KNAPP: My experience has not been any better than the preceding speaker's. I do not think that a trephining, if it is carefully performed, is necessarily to be condemned. The difficulty lies in determining the actual angle of the anterior chamber. As you all know, the trephine opening remains patent if Descemet's endothelium is included in the trephined area.

DR. IGERSHEIMER: Dr. Knapp, in which cases of juvenile glaucoma would you operate and in which would you not?

DR. KNAPP: The patient should be examined under a general anesthetic in order to determine the amount of damage done (cupping) to the optic nerve. Many of the eyes that we see are past the stage in which anything can be obtained by operation; upon the others I should operate.

QUESTION VII: IN YOUR SURGICAL EXPERIENCE WHICH OF THE FOUR TYPES OF OPERATION (ELLIOT, LAGRANGE, IRIDENCLEISIS, OR CYCLODIALYSIS) GAVE THE BEST RESULTS?

DR. KNAPP: I think the operation depends upon the condition. In early cases, in which the tension is only slightly elevated or can be reduced by drops, an iridectomy or a modified Lagrange would be the proper operation. If the tension is higher, but not over 35 mm. Hg. (Schiötz), a Lagrange operation is the best. Beyond that tension one has to take recourse in trephining. The advantage of the Lagrange is that the ectatic scar is avoided which so frequently follows an Elliot operation. If these operations are contraindicated a cyclodialysis can be done. I have had very little experience with iridencleisis.

DR. TÖRÖK: It is difficult to determine what operation one should perform in a case of glaucoma. In a general way it may be said that most ophthalmic surgeons prefer the broad iridectomy in cases of acute inflammatory glaucoma. Broad iridectomy is also performed in many cases of secondary glaucoma and preliminary to a cataract extraction, if glaucomatous symptoms are present.

Cyclodialysis is the operation for glaucoma simplex.

As to the Lagrange, trephining, and iridencleisis—they are performed in chronic inflammatory glaucoma, the choice depending entirely upon the surgeon.

Trephining is easier to perform and less dangerous than the Lagrange. However, the Lagrange seems to be preferable as the wound and filtering scar is placed in the sclera and is well protected by the upper lid. There is, therefore, somewhat less danger of the development of a late infection.

I have had no experience with iridencleisis, but I do believe that in this operation the closure of the filtering scar is more apt to occur than in either the Lagrange or trephining operation.

QUESTION VIII: DOES THE DIAGNOSIS OF GLAUCOMA MEAN INEVITABLE OPERATION?

DR. IGERSHEIMER: In cases of simple glaucoma in which there is tension, it is better to operate. Surgeons are not often unanimous in the decision whether to operate upon old people with simple glaucoma or not. There is no doubt that this process generally goes on with or without operation. Everybody has some good, some bad results from operating in such cases. It is very difficult or impossible to compare different eyes of different patients and to come to a definite conclusion. In this respect I think it is a good opportunity to be able to compare four comparable eyes. These eyes belonged to twins 75 years of age. When they came to me for the first time in 1927, there existed a glaucomatous cupping in all four discs. But the process had progressed further in the eyes of Baldwin than in those of Peter. You may see in the lantern slides the course of the disease.

BALDWIN

Left

1927 V: 0.2
Nasal visual field lost.
Tension 37 mm.
Trephine—Tension regulated.
1936 Identifies human forms.

Right

1927 V: 0.3
Bjerrum scotoma.
Tension 37 mm.
Trephining.
1928 Cyclodialysis.
1929 Tension regulated, but cataract.
1936 Light perception.

PETER

Left

1927 V: 0.9-1.0
Visual field normal.
Tension 32 mm.
1928 Bjerrum scotoma V: 0.7.
Cyclodialysis.
Tension regulated.
1935 Still able to read and write.

Right

1927 V: 0.9-1.0
Visual field normal.
Tension 37 mm.
1927-35 Only miotics.
1935 Totally blind.

In all four eyes there existed a progressive glaucoma simplex. The most interesting feature of these observations is that the right eye of Peter became totally blind, although in the beginning it was the best of all. This eye all these years had an ocular hypertension and was treated by miotics alone because the patient had refused an operation. The other three eyes had been operated upon, had a bad course, too, but not so bad as the eye not operated upon. So I think in cases of simple glaucoma that it is best to operate on old people also if there is an ocular hypertension, especially if the visual functions are good. But in simple glaucoma without hypertension, I do not see the real purpose of a decompressing eye operation. There are, of course, also cases of chronic inflammatory glaucoma, which are influenced very well by miotics and in which an operation can be delayed or avoided.

DR. SCHOENBERG: The question whether miotics are to be used over a long period of time can be answered in the affirmative only if we are certain that the patient or his relative knows how to use the drops properly and at the proper time. Stereotyped instructions as "use the drops, thrice daily" are worse than useless. In some patients, the tension rises around noon time, towards 4 to 5 p.m. or after the excitement from business transactions during the morning or early afternoon hours. In such cases, the drops are to be instilled about a half hour before going to business and at one to two o'clock in the afternoon. In other cases, the most important time to instill the miotics is at night just before retiring. The timing and frequency of instillations must be individualized in each patient.

QUESTIONS IX, X, AND XI: THE VALUE OF GRAPHS OF OCULAR TENSION. DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF DIURNAL VERSUS NOCTURNAL INCREASE OF OCULAR TENSION

DR. EVANS was asked to discuss the value of graphs of ocular tension and the practical value of provocative tests.

By way of answer he showed numerous graphical forms of recording the great variety of factors which have to be considered in the interpretation of glaucoma studies and presented a graph which is being tried out in the Department of Ophthalmology at the Long Island College Hospital.

Dr. Evans also showed that certain of the provocative tests are significant in one case and other tests more significant in another case. One case showed a sharp rise of the graph curves for coffee and not for the other provocative tests; whereas a number of cases were shown in which disturbance of the graph norms was most marked to water.

In order to interpret graphs, they have to show, besides the tension, visual acuity, blood pressure, visual field, and scotoma area, pupillary size, data on medication, and significant remarks.

DR. IGERSHEIMER: I think there is no doubt about the value of graphs of ocular tension but it is rather difficult to make reliable graphs without hospitalization of the patient. The real cause of the daily pressure-variations is not yet known. I

cannot believe that the rise of the ocular tension during the night is due to the horizontal position of the body or the size of the pupil. There is more evidence in favor of the theory that the eye movements have a pressure-decreasing effect. But, how is it with people in whom the climax of eye tension is not during the night, but at noon or in the afternoon? Hagen and also Sallmann have pointed out that this inverse type probably is not so rare as is generally believed. I show you here curves taken from pressure-variations in two young men with inverse types which are interesting from diagnostic, prognostic, and therapeutic points of view. The autonomic nervous system, perhaps also endocrine factors, may be important in such cases. The first patient, 22 years old, had had glaucomatous attacks in the left eye for about seven years. In this eye he showed the residua of an iritis and atrophic spots in the iris, but the pupil reacted well. These attacks occurred near noon, accompanied by cloudiness of the cornea, 50-mm. tension, and headache. The attack disappeared several hours afterwards. Antiglaucomatous therapy had no or only transient effect on the tension curve. In spite of the numerous attacks there was no ophthalmoscopic change and the vision, when there was no attack, was normal, probably due to self-regulation. The other patient was 21 years old, had been very myopic from his youth, and had had attacks of rainbows and cloudiness for four to five years. Proof that there was a glaucoma could not be brought out unless a real graph of the ocular tension of the left eye was taken. On this occasion it was found that: (1) there existed an inverse type of pressure variation; (2) the patient had a very strong reaction to miotics. There were no ophthalmoscopic signs of glaucoma, probably due to the self-regulation of the tension. The most important point in this observation is a therapeutic one. The patient formerly had his complaints especially on the right side. He used miotics in an irregular way. One evening as the cloudiness disturbed him more than usually he dropped 4-percent pilocarpine and eserine every hour into this eye. The next morning he had a detachment of the retina. In my opinion this was due to a very marked hypotony of the eye produced by the two factors: the normal decrease of the tension during the night and the strong effect of drugs. A knowledge of the above-mentioned facts would have forewarned us not to give strong miotics in such quantities especially in the evening.

QUESTION XII: WHAT IS THE PATHOGENESIS OF ACUTE GLAUCOMA?

DR. FRIEDENWALD:* Most fundamental to the understanding of glaucoma problems is the recognition that the congestive and noncongestive types represent two distinct entities. This was first conclusively shown by Rosengren, who observed that the shallow anterior chamber was characteristic of the congestive type alone, and was not present in eyes with glaucoma simplex that had not been operated on. He pointed out that the clinical recognition of the congestive type is often difficult since the congestive attacks may be limited in severity and transient.

Modern studies with the gonioscope have fully confirmed Rosengren's findings. It follows that the pathogenesis of congestive glaucoma is to be sought in connection with the cause of the shallowing of the chamber angle. A sufficient number of early cases have now been examined histologically to prove that the

* Although Dr. Jonas Friedenwald was detained from taking part in the round-table conference, he kindly consented to return written answers to the three questions submitted to him.

shallowness of the chamber angle in these cases is produced by a swelling of the anterior tips of the ciliary processes. This was first shown more than 50 years ago by Birnbaum but its significance was overlooked as long as the attempt was being made to explain congestive and noncongestive glaucoma on a unitary basis.

The swelling of the ciliary processes can be definitely attributed to the abnormality of the ciliary capillaries. This is proved by the fact that the interstitial fluid in the ciliary processes in these cases is infiltrated with plasma proteins which give it a hyaline appearance, and rings of fibrin can be demonstrated surrounding the capillaries. Moreover it has been shown that this pathological picture can be reproduced in animals by injecting capillary poisons into the vitreous. Furthermore, it has been shown that the intraocular fluid in acute glaucoma contains a capillary-active substance, possibly acetylcholine. The cause of the vasomotor disturbance and the source of the capillary-active substance still remain obscure.

In hemorrhagic glaucoma following retinal venous occlusion changes of an identical character are found in the ciliary body. It is to be presumed that in this case the source of the capillary-active substance is in the disintegrated retina.

Question XIII: What is the pathogenesis of glaucoma simplex?

Dr. Friedenwald: In respect to the pathogenesis of glaucoma simplex our position is a less happy one, and present knowledge is mainly of a negative character. Since the anterior chamber is not abnormally shallow in these cases, the hypothesis that the disease is due to a swelling of the vitreous is untenable. Furthermore the physical-chemical evidence on which the theory of swelling of the vitreous had been based has been shown to be false, and this conception has now been withdrawn by its chief proponents. Histological studies on the ciliary body in early cases failed to reveal any abnormality. This, however, does not suffice to rule out the possibility of increased rate of secretion in these cases, but no positive evidence for an enhanced rate of secretion has been brought forward.

Much attention has been concentrated on the histological features of the scleral-corneal trabeculum. Definite sclerosis of these fibers is often found, but this is not a regular feature of the earliest stages, and is probably to be interpreted as the result rather than the cause of the glaucoma. Some authors have suggested that a blocking of the drainage spaces occurs as the result of the accumulation of uveal pigment between the fibers of the scleral-corneal trabeculum. Both histological and gonioscopic studies suffice to rule this out as a cause of glaucoma.

If glaucoma simplex is not due to an increased rate of secretion of the aqueous, it must be due to a decreased rate of reabsorption, that is, to a decrease in the efficiency of action of Schlemm's canal. Within recent years it has been possible to show that the activity of Schlemm's canal as a reabsorbing mechanism is dependent on the inflow of blood into the canal from afferent arterioles, the reabsorption of fluid from the aqueous being effected by the protein osmotic pressure of the plasma in the canal. The rate of inflow of plasma into the canal is subject to elaborate vasomotor control. It seems possible, therefore, that a breakdown of this vasomotor control, perhaps through arteriosclerotic changes in the afferent arterioles, might produce the postulated inefficiency of the absorptive mechanism. Unfortunately the number of cases of chronic simple glaucoma available for histological study in the early

stages of the disease has been extremely limited, and a final answer on this point has been difficult to obtain.

QUESTION XIV: WHAT IS THE EFFECT OF OPERATION ON EYES SUFFERING WITH GLAUCOMA?

DR. FRIEDENWALD: The sudden lowering of intraocular pressure even in normal eyes produces an edema of the intraocular tissues which is most prominent in the ciliary processes. When an operation is performed on a glaucomatous eye, the stress placed upon the intraocular vessels is proportionately greater. As a consequence the postoperative edema of the ciliary processes may be quite marked even in cases of noncongestive glaucoma in which no abnormality of the ciliary capillaries precedes the operation. In the congestive type of the disease, the aggravating effect of operation on this anatomical feature is all the more marked. It follows that every operation for glaucoma in which the intraocular pressure is suddenly reduced must produce in varying intensity the anatomical equivalent of an attack of congestive glaucoma. Modern gonioscopic studies have shown that even in glaucoma simplex the chamber angle is frequently shallow postoperatively. Thus, operative interference even when successful tends to make the underlying pathological process of the glaucoma worse. It follows that if the creation of a filtering scar is unsuccessful, the glaucoma is usually much worse after operation than before. Perhaps one of the most hopeful features of current glaucoma investigations lies in the fact that the pharmacological control of this postoperative vasomotor disturbance presents no insuperable theoretical difficulties.

Sidney A. Fox,
Secretary.

AMERICAN JOURNAL OF OPTHALMOLOGY

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WILLIAM MACKENZIE

Perhaps the most interesting demonstration of progress in the science and art of medicine is to be had by reading the textbooks or medical journals of earlier years.

The best known of several excellent textbooks of ophthalmology which appeared in the early part of the nineteenth century was that of William Mackenzie, "lecturer on the eye in the University of Glasgow, and one of the surgeons of the Glasgow Eye Infirmary"; later "surgeon-oculist in Scotland to her Majesty" Queen Victoria.

Mackenzie's book went through a number of editions, and was translated into several European languages. It is still eminently readable, although sometimes provoking a smile by statements of principle or method which are no longer acceptable.

First published in England in 1830, the "Practical treatise of diseases of the eye" appeared in a first American edition in 1833, being issued by Carter, Hendee, and Company of Boston.

As illustrating the persistent popularity and steady growth of Mackenzie's treatise, it may be mentioned that, whereas the first American edition, dated 1833, contained only 719 pages, an edition published in 1855 by Blanchard and Lea of Philadelphia had 1027 pages of larger size.

Naturally there had been a distinct de-

velopment in knowledge regarding the eye even during the twenty-two years which elapsed between these two American editions. The volume of 1855 had acquired an "anatomical introduction explanatory of a horizontal section of the human eyeball," from the pen of Thomas Wharton Jones, the famous English surgeon who frankly confessed that he had rejected as worthless the first crude ophthalmoscope designed by the mathematician Babbage several years before Helmholtz' invention was made public.

This same later American edition, "from the fourth revised and enlarged London edition," contained numerous notes and additions by Addinell Hewson, "one of the surgeons to Wills Hospital for Diseases of the Eye."

Not infrequently the nomenclature of those earlier days (especially of 1833) differs materially from our own; in fact we are sometimes much exercised to understand what is meant by titles applied to certain supposed disease entities. How many American oculists of today have heard of grando, luscitas, aquo-capsulitis, albugo, or chrupsia? How many could define "acute idiopathic retinitis," a disease of the retina with external signs of inflammation; or crystalline-capsulitis et lentitis; or "noli me tangere"?

Even as late as 1855 pterygium was usually excised; lid cancer was quite respectably treated with iron carbonate or arsenic, although Mackenzie recommended the knife as more reliable; and solid lunar caustic was introduced into the lacrimal sac for the obliterative cure of dacryocystitis.

To "contagious ophthalmia" not much less space was devoted in the American edition of 1833 than in that of 1855. "From having passed," says Mackenzie in the earlier edition, "along with the British troops from Egypt to this country, in 1800, 1801, and 1802, it is often spoken of under the name of Egyptian ophthalmia." Some details of the description seem to suggest that more or less violent disturbances from several different causes were grouped together as manifestations of a single disease. As to etiology, both of the editions here mentioned use approximately the same language.

"Whether this disease be capable of propagating itself by infection, that is to say, whether the mere miasmata arising from the eyes of those affected with it, flowing through the air, be capable of exciting the same disease in the eyes of others, is a point which still remains in doubt." Reference is made (in a day when bacteriology was unknown) to accidental inoculation, group infection, and epidemics on board ship; with striking illustrative narratives. Another surgeon's attribution of the disease to erysipelas is refuted. A good deal of analogy to "catarrhal ophthalmia" is suggested; and it is interesting to note that Mackenzie regarded the exciting causes of catarrhal ophthalmia as being "atmospheric changes, and especially exposure to cold and wet."

Granular conjunctiva, or trachoma, is in both editions classified among "diseases consequent to the ophthalmiae." "I consider," says the earlier edition, "the prominences in question (granulations) to be principally the acini of the meibomian follicles in a state of enlargement." The edition of 1855 shows that this opinion had been abandoned: "The prominences in question are doubtless the villi or papillae of the palpebral conjunctiva, along with its grandular elements, hypertrophied and altered by chronic inflammation." "Granular conjunctiva may result from any of the puro-mucous ophthalmiae." In 1855 the British surgeon Lawrence is quoted as regarding granular ophthalmia as the effect of strong applications of nitrate of silver, "in salve or in

solution," in the puro-mucous ophthalmias.

It is not surprising that both the 1833 and the 1855 editions of Mackenzie's treatise devote extremely little space to refractive errors. Even in the later edition, asthenopia, considered as a disease, was attributed to many causes, among which refractive error fails to be included. In the 1833 edition, myopia and presbyopia ("presbyopia, or far-sightedness") were contrasted as two opposite conditions, approximately as myopia and hyperopia are contrasted today. We find mentioned, however, the fact that "young men of twenty sometimes cannot see to read or write without convex glasses of six or eight inches focus. . . ." "With regard to the efficient causes, flatness of the cornea from diminution in the quantity of the aqueous and vitreous humors is the one most frequently mentioned, this diminution being supposed to depend on the impeded manner in which the function of secretion is performed in advanced life."

Modern ophthalmologists would hardly be disposed to resort to the remarkable treatment for juvenile "presbyopia" which is recorded on page 609 of the 1833 edition. "Mr. Ware mentions the case of a boy of eight years old, who suddenly became presbyopic, and was repeatedly punished at school, on account of his incorrect and defaced writing. . . . After the presbyopia had continued a fortnight . . . cure was accomplished by the application of leeches to the temples, and the use of purgative medicines. Two sisters . . . were similarly affected. . . . The younger, a girl of fifteen, . . . in the course of six weeks, during which she totally abstained from the use of glasses, was completely relieved from the necessity of using them, by the application of two leeches to each temple twice a week."

As to astigmatism, the earlier edition is silent. Although the physicist Young had in 1801 called attention to the existence of such an irregularity of refraction (which he attributed to "an obliquity of the cornea and crystalline lens, with regard to the visual axis"), the subject seems hardly to have attracted any important amount of attention before the publication of Mackenzie's first edition.

In the 1855 American edition of Mackenzie's treatise, the two and a half pages devoted to an explanation of astigmatism are chiefly occupied with a record of the famous case of the astronomer Airy, who had presented the matter to the Philosophical Society of Cambridge, England, in 1827, and who in 1849 had put before the same Society a note as to the later changes which had occurred in his eye. In the meantime Whewell had proposed the term "astigmatism," and several other striking cases had been reported in the literature. This had led to the invention by Stokes, also of Cambridge, England, of the somewhat complicated piece of diagnostic apparatus upon which is based the simpler and more manageable cross cylinder of our own time.

W. H. Crisp.

GLAUCOMA SURVEY

In spite of the application of methods, devices, and procedures whereby the early diagnosis of glaucoma is at least theoretically possible, the fact remains that a depressing number of cases are undiagnosed until long after the disease has been established and irrevocable havoc has ensued.

The causes for this lag are to be found in a number of factors, among them being primarily the ignorance of the patient and consultant. This factor is potentially eradicable in time, and events of the recent past modestly show the result of the campaign for education of

the people, in that more and more of them are becoming mindful of what glaucoma means and does. At the same time, in the journals and societies, the consultant is bombarded with articles and papers on the various aspects of glaucoma, mostly scientific.

But it is not the ophthalmologist only who should be and generally is skilled in the diagnosis of this disease. Everyone, medical or nonmedical, to whom the patient may turn for advice should be taught to recognize this disturbance and refer him to the properly trained individual or ophthalmic clinic for treatment. It is admitted that the very early diagnosis of glaucoma is exceedingly difficult and that even well-trained ophthalmologists occasionally miss it. How much more difficult it is for the general practitioner and the optometrist to recognize the early stages, every ophthalmologist can cite from his own experience. It is hard to believe that anyone would deliberately allow a patient to become totally blind except through ignorance, just for the sake of selling more and more glasses. But such ignorance is criminal and constitutes malpractice. The teaching of the consultant is the responsibility of ophthalmology, and for that reason conscientious ophthalmologists welcome the rescinding of the resolution against the teaching of optometrists at the last meeting of the Section on Ophthalmology, A.M.A.

That the problem is still more broad, however, is becoming evident through the recent work of Dr. Mark J. Schoenberg of New York, and the National Society for the Prevention of Blindness. In a series of papers recently presented before the American Ophthalmological Society and the American Academy of Ophthalmology and Otolaryngology, Dr. Schoenberg gave reports on surveys of glaucoma records from three large New York eye clinics. The findings were summarized and the prevailing weaknesses of the present system of diagnosis and treatment of glaucoma patients in the eye clinics, were pointed out. Remedial measures were suggested that at first glance seem to be too theoretical, impractical, and difficult of undertaking, involving as they do the compiling of records and follow-up activities by social workers, the services of more ophthalmologists than appear available, and the expenditure of more money than is generally at hand. The broad scope is too dazzling and the tired worker discouraged. But this gloomy prognosis can be swept away by dogged determination, not by the individual but only through the activities of the various ophthalmic organizations acting as a body. The National Society for the Prevention of Blindness has undertaken the sponsorship of this magnificent work. Their campaign for the reduction of the percentage of partial or total loss of vision from glaucoma not only invites but demands the support and coöperation of not only ophthalmologic organizations but also those of the optometric and public health bodies. With a clear vision of what is required, such coöperation and support will be forthcoming.

Derrick Vail.

BOOK NOTICE

THE PRINCIPAL NERVOUS PATHWAYS. By Andrew Theodore Rasmussen, Ph.D. Second edition. 73 pages, index, and numerous illustrations. New York, The Macmillan Company, 1941. Price $2.50.

The first edition of this book was published in 1932. Eight pages are concerned with the eye. Four of these are occupied by diagrammatic figures. The first concerns binocular vision and re-

flexes through the midbrain. The second, localization of fibers from the retina to the visual cortex. The third, innervation of the eye, and the fourth, the visual system. The text figures are clear and illustrate the visual mechanism satisfactorily. The entire book would be valuable to the student of ophthalmo-neurology as well as of neurology in general.

Lawrence T. Post.

OBITUARIES

JOSEPH A. WHITE

1848-1941

On February 16, 1941, Dr. Joseph A. White of Richmond, Virginia, one of the earliest specialists in the South, died in his ninety-third year.

Dr. White, dean of eye, ear, nose, and throat specialists of the South Atlantic seaboard, was born in Baltimore on April 19, 1848. He received his early education in the parochial schools in Baltimore and later attended college at Rock Hill College, Loyola College, and St. Mary's College, and from the latter institution he received the degree of Master of Arts. From this institution he entered the University of Maryland, where he was graduated from the medical department in 1869. Wishing to pursue his training in medicine further, he then went for study at the École de Médecine, Paris, France, and at the Universities of Baden, Heidelberg, and Berlin, Germany.

In 1872, Dr. White returned to Baltimore to practice general surgery. During the next few years he gradually began to limit his practice to diseases of the eye, ear, nose, and throat, and seven years later he located in Richmond, Virginia, to confine himself entirely to this speciality. He often stated that his reason for leaving Baltimore was that there was not room in Baltimore for two such specialists as Dr. Chisholm and himself.

In Richmond, Dr. White very quickly established a large practice, since conditions connected with his speciality, up to that time, had been more or less neglected. His skill and his personality soon won for him wide recognition, and for over 60 years he continued a busy, progressive, and lucrative practice.

Aside from his private practice, he spent much time at his own private clinic, which he founded and which was operated exclusively for the care of indigent patients. For many years he was active in teaching, first at the University College of Medicine and later at the Medical College of Virginia when the two schools merged in 1913. His lectures were most interesting. His charming personality combined with his witticisms, personal experiences, and his succinct phraseology held the close attention of his students. He frequently used lantern slides to demonstrate his lectures and occasionally "by mistake" a slide of some Parisienne model would get among his medical slides, much to the delight of his students.

Dr. White was a frequent writer of medical papers. He contributed not only to the journals of his speciality but to journals that would bring special messages to general practitioners and others. Although his articles were not long they were well expressed, and always brought forth some progressive idea. About 60 different reprints of his articles are in existence but it is highly possible that he wrote over three times that number.

Dr. White's charming personality and his keen intellect brought to him many posts of honor in the national societies. In 1884 and 1885 he was chairman of the Section on Ophthalmology of the American Medical Association, later president of the American Laryngological, Rhinological, and Otological Society, president of the Tri-State Medical As-

sociation of the Carolinas and Virginia, president of the Richmond Academy of Medicine, and president of the Medical Society of Virginia. He was also honored by membership in the American Otological Society and the American Ophthalmological Society.

Dr. White originated the most commonly used antiseptic ointment in ophthalmology (White's ointment).

There has been no operator with whom I have come in contact who had the calm assurance possessed by Dr. White. He studied his cases carefully before operation, he operated with great dexterity, and when the operation was completed he left with the feeling that he had done his best, and no worries attended his mind after office hours. He expected his patients to do well after an operation but if they did not he was not perturbed.

One remarkable attribute of this noted physician was his continued youthful enthusiasm for all progressive things in ophthalmology and to a lesser extent in otolaryngology. During the past few years of his life he continued to read widely, subscribing to the best journals of this country, of France, and of Germany and digested them with thoroughness. Even beyond the age of four score he adopted the newer operations devised by others and acquired new instruments to perfect his skill in these operations. He sought companionship of his youthful associates and was always eager to teach them and equally eager to learn from them.

He was a leader in the civic and social life of Richmond for several decades, since he was an artful dancer, brilliant conversationalist, and always a perfect gentleman.

Through the death of Dr. White the South Atlantic States have lost an outstanding leader in his profession, and it is difficult to realize that such a dynamic personality has been removed from his field of long usefulness.

Robert H. Courtney.

THOMAS ADAMS WOODRUFF

1866-1941

It is my sad duty to report the death of our old and valued friend, Thomas Adams Woodruff.

Dr. Woodruff died at his home in New London, Connecticut, on April 15th, after a lingering illness. He was seventy-five years of age.

His medical career covered a period of 50 years, the first four years of which were spent in general practice in Chicago. For 23 years thereafter he confined his practice to ophthalmology in Chicago. In 1918 he went to New London, Connecticut, where he lived and continued to practice his specialty until the time of his death.

Dr. Woodruff was born in St. Catherines, Ontario, on June 4, 1865, the son of Samuel DeVeaux Woodruff and Jane Sanderson Woodruff.

His early education was acquired at the Upper Canada College in Toronto. He took his M.D. and C.M. degrees at Magill University in 1888. Postgraduate work followed in Berlin, Vienna, Göttingen, and in London, where in 1890 he became a Licentiate of the Royal College of Physicians.

During the 27 years of his practice in Chicago he was perhaps best known in the Chicago Ophthalmological Society, of which he was president in 1908.

He served as ophthalmic surgeon on the staffs of St. Luke's and St. Anthony de Padua Hospitals, and for many years held the post of editorial secretary of the Ophthalmic Record.

He held the rank of Major in the United States Army Medical Corps, and

in 1917-18 served as head of the eye department of the base hospital at Camp Grant, Illinois.

Later he was chief of the section of surgery at the base hospitals at Camp Beauregard, Louisiana, and Camp Meade, Maryland.

In 1914 he married Caroline M. Wright, and in 1918 they moved to New London, Connecticut, where he served as consulting ophthalmologist to the Lawrence and Memorial Hospitals.

Dr. Woodruff made many contributions to the literature of his specialty. He was co-author with Dr. Casey A. Wood of "Common diseases of the eye."

He was a Fellow of the American Medical Association, which he served as third vice-president in 1908. He was also a Fellow of the American College of Surgeons; a member of the American Academy of Ophthalmology and Oto-Laryngology; a member of the Illinois State Medical Society; the Chicago Medical Society, and the Chicago Ophthalmological Society.

He was also a member of the Connecticut State Medical Society, Zeta Psi fraternity, and the Military Order of Foreign Wars. His activities in New London included membership in the Chamber of Commerce, the Rotary Club, the Thames Club, of which he was a past president, and the Shenecossett Country Club.

He is survived by a daughter, Mrs. John Wilbur of New London, and a grandson, John W. Ogden of Oakland, California.

Although he has not lived among us for many years he is still remembered with affection for his charming personality and with respect for his ability and for the place he achieved in his chosen field.

Frank T. Brawley.

ABSTRACT DEPARTMENT

EDITED BY DR. WILLIAM H. CRISP

ASSISTED BY DR. GEORGE A. FILMER

Abstracts are classified under the divisions listed below, which broadly correspond to those formerly used in the Ophthalmic Year Book. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. General methods of diagnosis
2. Therapeutics and operations
3. Physiologic optics, refraction, and color vision
4. Ocular movements
5. Conjunctiva
6. Cornea and sclera
7. Uveal tract, sympathetic disease, and aqueous humor
8. Glaucoma and ocular tension
9. Crystalline lens
10. Retina and vitreous
11. Optic nerve and toxic amblyopias
12. Visual tracts and centers
13. Eyeball and orbit
14. Eyelids and lacrimal apparatus
15. Tumors
16. Injuries
17. Systemic diseases and parasites
18. Hygiene, sociology, education, and history
19. Anatomy, embryology, and comparative ophthalmology

1

GENERAL METHODS OF DIAGNOSIS

Bogart, D. W. **An improved binocular gonioscopic apparatus.** Arch. of Ophth., 1941, v. 25, April, pp. 669-671.

To the author's original apparatus, which is suspended in a large panoramic tripod head with all motion controlled by the action of a heavy lever, has been added a Barkan lamp for illumination. (Illustrations.)

J. Hewitt Judd.

Caveness, H. L., Satterfield, G. H., and Dann, W. J. **Correlation of the results of the biophotometer test with the vitamin-A content of human blood.** Arch. of Ophth., 1941, v. 25, May, pp. 827-832.

Biophotometer readings and fasting blood-plasma levels of vitamin A were determined for 71 subjects; for nine of them the readings were repeated after five-days administration of a supplement of vitamin A. Only a slight correlation was found between the biophotometer readings and the levels of vitamin A in the blood.

J. Hewitt Judd.

Evans, J. N. **The new scotometer.** Arch. of Ophth., 1941, v. 25, March, pp. 445-449. (See Amer. Jour. Ophth., 1941, v. 24, June, p. 714.)

Friedman, Benjamin. **An improvement in the gonioscope contact glass to facilitate filling with fluid.** Arch. of Ophth., 1941, v. 25, March, p. 510.

In order to fill a contact glass with fluid while the glass remains in position on the patient's eye, two narrow channels are drilled through it, one at the center, and one 2 mm. away. Solution is injected through the eccentric hole and the air escapes through the central one. J. Hewitt Judd.

Hopkins, C. R. **Size and location of the blind spot of Mariotte.** Arch. of Ophth., 1941, v. 25, May, pp. 811-813.

The general variation in the figures obtained in this study of one hundred angioscotometric records from those given by previous authors using different techniques indicates a larger blind spot. This is obviously due to a number of causes besides variation of light, such as size of the test object and contrast to the background. Immediately

adjacent to the zone of absolute blindness at the blind spot is a narrow zone in which the 2/2,000 isopter may not be plotted. This is said to be due to the reduced number of rods and cones in the peripapillary area but may be due to the defect arising from the effect of the vascular circle of Zinn and its associated perivascular mechanism.

J. Hewitt Judd.

Longhena, Luisa. **Blood-sedimentation rate in ocular disease.** Rassegna Ital. d'Ottal., 1940, v. 9, Nov.-Dec., pp. 665-687.

The author reviews the knowledge of blood sedimentation and the literature pertaining to ophthalmology. She examined 119 cases of ocular disease and found that the sedimentation rate was strongly increased in acute inflammatory, rheumatic, luetic, and late neoplastic diseases, moderately in tuberculous disease, and not at all in trachoma, glaucoma, cataract, and retinal separation. Eugene M. Blake.

Mitzkevich, L. D. **Intravenous administration of hypertonic salt solution to demonstrate the malarial nature of ocular diseases.** Viestnik Opht., 1940, v. 17, pt. 5, p. 648.

The author suggests that 10 to 20 c.c. of 15-percent saline be administered intravenously in ocular diseases of suspected malarial etiology in which the parasite cannot be demonstrated in the blood. After such provocative injections the parasite may appear in the blood without causing a general malarial attack. Ray K. Daily.

Rugg-Gunn, A. **A new binocular ophthalmoscope.** Trans. Ophth. Soc. United Kingdom, 1940, v. 60, p. 195.

A new binocular ophthalmoscope whose general principle is similar to the Gullstrand is presented.

Beulah Cushman.

Vishnevskii, H. A. **Angioscotometry and its diagnostic significance.** Viestnik Opht., 1940, v. 17, pt. 5, p. 571.

A review of the literature and an analysis of data obtained on 311 patients. The data show physiologic as well as pathologic variations in the size of angioscotoma. Angioscotomata change in size in glaucoma, neuritis, retrobulbar neuritis, and vascular retinal disease. The most marked changes in the size of the scotoma are found in chronic glaucoma and optic neuritis. There is no constant relation between the size of the blind spot, visual acuity, or intraocular tension and the size of the scotoma. For diagnostic purposes the comparison of the angioscotoma in the two eyes is more valuable than a unilateral determination. (Illustration.) Ray K. Daily.

2

THERAPEUTICS AND OPERATIONS

Arcuri, Domenico. **The effect of short-wave therapy upon normal and diseased eyes.** Rassegna Ital. d'Ottal., 1940, v. 9, March-April, pp. 232-242.

Of 120 persons treated by short-wave therapy, ten were cases of uveitis with hypertension and forty were cases of glaucoma of various types. In no case was there an increase of intraocular tension, and, therefore, such treatment is not contraindicated. Definite improvement in uveitis is reported with reduction in complicating tension. All cases were treated by ultrashort waves of 6 meters for 20 minutes at each treatment. Eugene M. Blake.

Askalonova, T. A., and Vilovskaja, K. E. **The eyeball after prolonged administration of plasmocide.** Viestnik Opht., 1940, v. 17, pt. 5, p. 630.

Carefully controlled therapy of 523 patients led to the conclusion that in therapeutic doses acrichinin and plasmocide were harmless to the eye and were as effective as quinine.

Ray K. Daily.

Berrettini, G. L. **Mydriatic and cycloplegic principle existing in "trombeteira" (Datura arborea and D. fastuosa L.).** Arquivos Brasileiros de Oft., 1941, v. 4, Feb., pp. 50-59.

A boy of 11 years, seeking to gather flowers from a forest tree, brought his face into contact with a part of the tree, which injured his left eye. A small piece of the flower was found in the lower cul de sac. Pupillary action was abolished, the accommodation greatly weakened. The action of preparations of the plant was studied in dogs. It was approximately identical with that of Datura stramonium.

W. H. Crisp.

Bossalino, G., and Sironi, L. **Tuberculous affections of the eye and tuberculin therapy.** Rassegna Ital. d'Ottal., 1940, v. 9, March-April, pp. 161-200.

The authors review the history of ocular tuberculosis from 1858 and describe 38 cases illustrating involvement of the various ocular tunics. They conclude that the skin reaction to tuberculin signifies a hypersensitivity to the tuberculin itself and that the use of very small doses, gradually increased in strength, produces a desensitization, adjusting the allergic state to the tuberculous antigen. The authors believe that the reason for the value of small doses of tuberculin is somewhat indeterminate, but that the results are satisfactory. (11 figures.)

Eugene M. Blake.

Calvery, H. O., Lightbody, H. D., and Rones, B. **Effects of some silver salts on the eye (silver nitrate, silver ammonium nitrate, silver ammonium sulphate, silver ammonium lactate and a mixture of silver ammonium nitrate and silver ammonium sulphate.** Arch. of Ophth., 1941, v. 25, May, pp. 839-847.

The physiologic effects of solutions of 1 to 12 percent of silver nitrate and equimolecular solutions of silver ammonium nitrate and silver ammonium sulphate, silver ammonium lactate, and ammonium boric acid chloride in distilled water have been observed upon the eyes of rabbits. Comparative effects were noted in all instances after instillation of a single measured drop in the lower culdesac of the left eye, the right eye serving as control. The results clearly show that ammonium salts are more injurious than silver nitrate. This is due to the fact that the silver ammonium salts are very reactive, so that when they come in contact with fluids and tissues of the eye, silver ions and ammonia are immediately released. The liberated ammonia is itself a strong irritant, injuring the tissues of the eye to some extent. Silver salts in all concentrations used were irritating to the eyes of rabbits, the degree of irritation being dependent upon the concentration as well as the nature of the salts being tested. Dark silver deposits may result from a single application of silver salts to the eye. Therefore, silver salts should not be used in the eye except when absolutely necessary, and then with extreme caution.

J. Hewitt Judd.

Harrison, W. J. **A new container for ophthalmic ointments.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 933-934.

Miklos, A. **Contribution to the chemotherapy of tuberculosis of the eye.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 20-36.

Remarkable results in the treatment of ocular tuberculosis were obtained with Rubrophen, an organic dye. The drug was injected in a dose of 0.3 gm. and given internally in tablets of 0.15 gm. 4 to 6 times daily. The report concerns 50 cases, among them iritis, periphlebitis retinalis, keratoconjunctivitis, and one case of sympathetic ophthalmia. Gertrude S. Hausmann.

Mitzkevich, L. D. **Evaluation of the bactericidal properties of ophthalmic ointments.** Viestnik Opht., 1940, v. 17, pt. 6, p. 775.

A laboratory study, the results of which show that ointment of yellow oxide of mercury is the most bactericidal of the ophthalmic ointments in use. Ointments of soluble mercury salts and protargol depend for their action on long contact with the conjunctiva. Zinc sulphate is bactericidal only to Morax-Axenfeld bacilli.

Ray K. Daily.

Pinho, Edson. **Iris prolapse. Trichloracetic acid.** Arquivos Brasileiros de Oft., 1940, v. 3, Dec., pp. 304-305.

Pinho briefly extols the use of a saturated solution of the drug for this condition, the application being made with the end of a toothpick, daily for a week, under local anesthesia.

W. H. Crisp.

Saubermann, G. B. C., and Schmid, A. E. **The use of irgamid, a sulfanilamide derivative, in ophthalmology.** Ophthalmologica, 1941, v. 101, April, p. 193.

On the basis of their experience in the treatment of more than seventy patients with infectious diseases of the eyes, the authors recommend irgamid. The course was often shortened astonishingly in serpent and other corneal ulcers, intraocular traumatic infection, dacryocystitis, lid phlegmon, and gonorrheal conjunctivitis. It is also believed that inclusion-body conjunctivitis is favorably influenced. In serpent ulcer the addition of irgamid to standard therapeutic procedures was so gratifying that the authors were encouraged to rely on irgamid as the mainstay. F. Herbert Haessler.

Saubermann, G. B. C., and Schmid, A. E. **Treatment of scrofulous eye disease with a sulfanilamide compound (cibazol).** Ophthalmologica, 1941, v. 101, April, p. 201.

In ten patients with scrofulous ocular affections, signs of irritation, phlyctenules, and corneal infiltrates disappeared in a few days after beginning the use of a 5-percent-cibazol ointment three or four times daily.

F. Herbert Haessler.

Seidenari, Renato. **Sulfonamide therapy in ophthalmology.** Rassegna Ital. d'Ottal., 1940, v. 9, March-April, pp. 200-216.

Thirty-one cases of ocular disease, including trachoma with pannus, purulent dacryocystitis, gonococcal conjunctivitis, phlegmon of the lids and orbit, and panophthalmitis, were treated with sulfanilamide. The author reviews the literature pertaining to each condition with the results of treatment, which

were favorable in most conditions. Keratitis with hypopyon did not respond at all. Eugene M. Blake.

Statti, L. W. **Pentothal sodium anesthesia in ophthalmology.** Arch. of Ophth., 1941, v. 25, March, pp. 487-490.

Favorable results in one hundred consecutive cases, in which all types of ophthalmic surgical procedure were carried out on patients whose general physical conditions and ages varied widely, furnish the basis for the author's conclusion that pentothal sodium injected intravenously is an ideal anesthetic, easy to administer and rapid in effect. The postoperative reaction time is brief and there are no serious complications. J. Hewitt Judd.

Veasey, C. A., Jr. **Vitamin B in ophthalmology.** Arch. of Ophth., 1941, v. 25, March, pp. 450-468.

The various components of the water-soluble group of vitamins are briefly defined, and the ocular effects of avitaminosis B are fully reviewed with respect to both clinical ophthalmology and experimentation on laboratory animals. Subclinical avitaminosis B is widespread. Benefit may be expected from vitamin therapy in cases of toxic amblyopia, retrobulbar neuritis, certain corneal conditions, Wernicke's disease and similar depletion syndromes, and possibly in cases of uveitis and chorioretinal involvement of unknown cause. Administration of riboflavin will arrest cataracts in riboflavin-deficient animals, but there is no evidence of a similar effect occurring in humans, with the possible exception of the arrest of the swelling of the lens in cases of intumescent senile cataract. Ten illustrative cases are reported.

J. Hewitt Judd.

3

PHYSIOLOGIC OPTICS, REFRACTION, AND COLOR VISION

Alexander, G. F. **Spasm of accommodation.** Trans. Ophth. Soc. United Kingdom, 1940, v. 60, p. 207.

Spasm of accommodation as described by the author is usually found in young subjects doing much near work. Minus lenses correct the visual acuity but do not relieve the discomfort. The following factors are considered in the study of spasm of accommodation: astigmatism arising from constant variation in the activity of the ciliary muscle in the attempt to see different meridional aspects of objects distinctly; throwing the light into the eye by the mirror in doing skiascopy without cycloplegia; exophoria; and myopia. The use of one drop of 16-percent homatropine solution as a cycloplegic is advocated. The discussion following the article is critical of the diagnosis and technique.

Beulah Cushman.

Blankstein, S. S. **Transitory myopia (complication of sulfanilamide therapy).** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 895-899.

Broda, E. E., and Victor, E. **The cataphoretic mobility of visual purple.** Biochem. Jour., 1940, v. 34, Dec., p. 1501.

This rather technical article shows the results of experiments on this photosensitive substance made in a safe red light. Varying exposures and resulting reaction velocities are enumerated in an accompanying table.

F. M. Crage.

Chuprakov, A. T. **The influence of dark objects in the visual field on the**

differentiation sensitivity of the fovea. Viestnik Opht., 1940, v. 17, pt. 5, p. 680.

This laboratory investigation demonstrates that the presence of a dark ring in the visual field diminishes foveal sensitivity. The influence of the peripheral object increases with its size, with its proximity to the fovea, and with the resultant loss in illumination. This effect is produced also by placing the dark ring in the field of the other eye, which indicates that the process is central in origin.

Ray K. Daily.

Cogan, D. G. **Some ocular phenomena produced with polarized light.** Arch. of Ophth., 1941, v. 25, March, pp. 391-400.

The author describes two ocular phenomena produced with polaroids. The first is exhibited by the lens and consists of a dark cross on a light background. The second phenomenon, which has not been described previously, is exhibited by the anterior segment of the intact eye, and consists of a dark cross seen against a light background. It is produced by the normal cornea and, like the lenticular cross, depends on a radial or concentric arrangement of the elements, and not upon increased intraocular pressure.

J. Hewitt Judd.

Cotlier, I. **Astigmatic accommodation.** Anales Argentinos de Oft., 1941, v. 2, Jan.-Feb.-March, pp. 6-36.

This 31-page article, accepting the belief that there is an astigmatic accommodation due to unequal action of the ciliary muscle, proceeds to describe the behavior of a number of subjects in looking at the astigmatic dial through various lens combinations. The author approves the "bicylindric" technique of Màrquez, and urges the investigation of small fractions of astigmatism. (Bibliography.)

W. H. Crisp.

Cusick, P. L., and Hawn, H. W. **Prism compensation in cases of anisometropia.** Arch. of Ophth., 1941, v. 25, April, pp. 651-654.

Although in many cases of moderate and even high degrees of anisometropia, prism compensation is unnecessary for comfort, others have a definite need for compensating prisms to obviate asthenopia which, at times, simulates an ocular neurosis. The presence of poor vision in one eye does not obviate the necessity for compensation if binocular single vision is shown to be present. The authors treat these conditions as a hyperphoria in downward gaze due to a muscle defect. After repeated measurements with the Maddox rod at the individual working distance, clip-on lenses with divided prisms are prescribed for a month's trial. If relief is obtained, a compensated prism bifocal or slab-off lens is prescribed. Two cases illustrative of this condition are reported. The amount of prism indicated by this method is less than the amount indicated mathematically when 8 or 10 mm. is taken arbitrarily as the amount of depression of the eyes in downward gaze. J. Hewitt Judd.

Eidelman, B. M. **Rabkin's polychromatic plates.** Viestnik Opht., 1940, v. 17, pt. 5, p. 658.

An evaluation of these plates from the standpoint of reliability, sensitivity, and accuracy of differential diagnosis. The material consisted of one hundred normal persons and seventy persons with various color anomalies. The conclusions are that in the detection of protanopes Rabkin's plates are superior to Ishihara plates, are equally

reliable in the diagnosis of deuteranopes, but are inferior in the diagnosis of anomalous trichromats.

Ray K. Daily.

Filatov, V. P., and Volokitenko, A. E. **Osmotherapy in high myopia without macular changes.** Viestnik Opht., 1940, v. 17, pt. 5, p. 515.

Twenty-four cases of high myopia were treated with intravenous injections of 10-percent saline with satisfactory results. Visual acuity improved in all cases, and in some there was an extension of the visual fields.

Ray K. Daily.

Friedman, B. B. **Acute myopia induced by sulfanilamide.** Amer. Jour. Ophth., 1941, v. 24, Aug., p. 935.

Heglo, L. G. **An evaluation of the Rabkin, Stilling, and Ishihara plates used in artificial light.** Viestnik Opht., 1940, v. 17, pt. 6, p. 824.

A graphic report of this investigation shows that in artificial light the results obtained with Rabkin or Stilling plates are accurate, whereas the Ishihara plates are unreliable.

Ray K. Daily.

Luckiesh, M., and Moss, F. K. **Characteristics of sensitometric refraction.** Arch. of Ophth., 1941, v. 25, April, pp. 576-581.

The relations between visibility and refraction and accommodation and convergence are presented in detail for a typical adult emmetropic subject. These relations not only indicate the relative extent to which vision is blurred by various refractive errors, but also reveal the progressive changes in the refractive state of the eyes concomitant with binocular convergence at various fixational distances between infinity and the near point. The data are particularly significant because all determinations of the refractive states of the eyes are based on the absolute and fundamental criterion of maximal visibility rather than on some arbitrary standard of normal visual acuity. A high degree of precision is obtained by repeating under identical physical conditions the quantitative measurements of visibility, so that each measurement quantitatively influences the final result. From the evidence so far obtained it appears that the refractive errors indicated by dynamic sensitometry are of the same type and amount as those indicated by the usual methods after the induction of cycloplegia or by fogging. The sensitometric data are held to be more readily interpretable because they are obtained with binocular convergence and under conditions of normal nervous control of the ocular musculature. Thus the sensitometric method adds a subjective test which is at least as significant and precise at all distances as are present static tests, either under conditions of normal muscular control or after the induction of cycloplegia. Furthermore, sensitometric examinations at critical distances provide data for determining the direction and the extent of the relative accommodation which will be required with any prescribed correction and at any distance. J. Hewitt Judd.

Ludvigh, Elek. **Effect of reduced contrast on visual acuity as measured with Snellen test letters.** Arch. of Ophth., 1941, v. 25, March, pp. 469-474.

The author finds that at low levels of contrast, visual acuity varies markedly with contrast, but at high levels of contrast, relatively great

changes in the degree of contrast have slight effect upon the visual acuity. Hence, if the test letters and the background of a Snellen chart provide reasonably high contrast (above approximately 60 percent) the relatively slight variations attributable to differences in manufacture will have little effect on the visual acuity. In the absence of further evidence, one should not assume that the spectacle lens which produces the greatest contrast sensitivity will also produce the greatest visual acuity according to the Snellen test at high contrasts. It is also stated that the low visual acuity in amblyopia ex anopsia cannot be attributed to defective light-difference sensitivity as this may be normal or reduced relative to the unaffected eye. The central scotoma, which is frequently found in patients with amblyopia ex anopsia, does not suffice to account for the observed low acuity. J. Hewitt Judd.

Mattos, W. B. **Editing a prescription for glasses.** Arquivos Brasileiros de Oft., 1941, v. 4, June, pp. 143-146.

The author apparently continues to employ the mode of indicating axis adopted many years ago at the Naples International Congress, namely vertical, horizontal, or so many degrees nasal, temporal, and so on. He reproduces, with the statement that it is incomprehensible, a prescription in which the cylindric axes are indicated by the simple numbers "105" and "75," in accordance with the convenient practice so long in use in the United States. He will shock most United States oculists by his assertion that it is quite unnecessary for the oculist to inspect the lenses as to their accuracy after the optician has ground and mounted them. W. H. Crisp.

Paez Allende, Francisco. **Myopia from ingestion of p-amino benzol-sulfamide.** La Semana Med., 1941, v. 48, May 29, p. 1273.

The drug was administered on account of eczema of both thighs induced by a rubber bandage. After the second dose the patient reported a great reduction in distant vision, and she was found to have myopia of 3 D. in each eye. Improvement in vision proceeded rapidly after discontinuance of the drug, and after four days the refraction was emmetropic. W. H. Crisp.

Pascal, J. I. **Practical applications of dynamic retinoscopy.** Arch. of Ophth., 1941, v. 25, May, pp. 859-862.

Since dynamic retinoscopy is done while the eyes are accommodating and converging actively, it provides a method of measuring objectively the near-point of accommodation, the amount of residual accommodation, and the depth of cycloplegia; allows a comparison of the quantity and quality of the accommodation of the two eyes; and gives a check for overcorrection in cases of myopia. One advantage claimed by the author is that the eyes may be examined while they are engaged in natural binocular vision and each eye may be studied while both eyes are engaged in the act of seeing.

J. Hewitt Judd.

Prado, Durval. **Considerations regarding asthenopia.** Arquivos Brasileiros de Oft., 1941, v. 4, June, pp. 133-136.

The author discusses the heterophorias mainly as symptomatic of uncorrected refractive error. W. H. Crisp.

Rabkin, E. B., and Heglo, L. G. **Types of color blindness.** Viestnik Opht., 1940, v. 17, pt. 5, p. 637.

A review of the literature and a report of the author's own investigation, on the basis of which he proposes to modify Kries's classification by subdividing protanomaly and deuteranomaly into types A, B, and C. In type A there is a displacement of the color perception curves on the Nagel anomaloscope. In types B and C there is a deformation of the curves, less pronounced in type C than in B.

Ray K. Daily.

Roslavtzev, A. V. **Contrast sensitivity in normal trichromats and in people with anomalies of color vision.** Viestnik Opht., 1940, v. 17, pt. 5, p. 663.

The objective of this study was to determine the suitability of people with color defects for work in the heat departments of the metal industry, where the degree of heat is judged by the appearance of the heated metal. The conclusion is that contrast sensitivity in people with color anomalies is equal to that of normal trichromats.

Ray K. Daily.

Saba, Gaetano. **Transient myopia in sulphonamide therapy.** Rassegna Ital. d'Ottal., 1940, v. 9, Nov.-Dec., pp. 708-718.

The author discusses sulphonamide therapy and its complications in ocular diseases. He believes that the transient myopia observed at times is the result either of spasm of the ciliary muscle or of an increase in the index of refraction of the ocular media, particularly the aqueous. Eugene M. Blake.

Scardaccione, Mario. **The action of the different vitamins on the light sense in man and the migration of the retinal pigment.** Bollettino d'Ocul., 1940, v. 19, Feb., pp. 121-147.

The actions of vitamins A, B_1, B_2, C, D, and E were tested. Vitamins A and B_1 seemed to increase the light sense in patients affected by a low light sense or by hemeralopia from avitaminosis. Vitamin C provoked the light position in the eyes adapted to darkness. (Bibliography.)

M. Lombardo.

Simpson, R. K. **Combination of phorometer and accommodation rule.** Arch. of Ophth., 1941, v. 25, March, pp. 483-486.

The instrument consists of a rotary prism and Maddox rod from a phorometer trial-frame, mounted on a handle, on one side of which is a millimeter rule for measuring interpupillary distance, point of convergence, and so on, and on the opposite side a dioptric scale and the Duane table of accommodation as to age. J. Hewitt Judd.

Weber, E. **The refractive errors of twins.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 78-83.

Weber reports several cases of twins with nearly identical refractive errors. The cases tend to establish the hereditary origin of refractive errors.

Gertrude S. Hausmann.

4

OCULAR MOVEMENTS

Alvaro, M. E. **Surgical treatment of strabismus.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 1-113.

This detailed review of the subject covers 113 pages (Portuguese). It is divided into the following sections: historical, generalities, operative indication, operative technique. Each section carries its own bibliography, and the whole article includes 63 illustrations.

W. H. Crisp.

Andrade, Cesario de. **Brief considerations on the etiopathogenesis and treatment of strabismus.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 180-189.

For re-education of binocular vision, the author recommends exercises with spectacles of complementary colors. Looking at a luminous source through a perforated screen, the patient with a deviating eye fails at first to see the light through the red glass placed in front of this eye, whereas he sees the light through the green glass placed over the good eye. Rapid alternate covering of each eye leads to the moment at which the patient is able to see both colored images at the same time. The patient then gradually learns to fuse the two images by relaxing or increasing his convergence. By means of another simple apparatus described by the author, and in which is incorporated a mechanical contrivance for uncovering either eye at will by pulling a string, the patient is able to take charge of his own exercises.

W. H. Crisp.

Brückner, R. **A hitherto undescribed ocular symptom of ophthalmoplegic migraine.** Ophthalmologica, 1941, v. 101, Feb., p. 91.

Ophthalmoplegic migraine is a symptom complex characterized by partial or complete paresis of the oculomotor nerve, and occasionally of the abducens and trochlear nerves, and associated with headache, gastric manifestations, and sometimes scintillating scotoma. It is observed as an essential (cryptogenetic) migraine or as produced by intracranial neoplasm, aneurysm, or arachnoiditis. The essential form is believed to result from transient vasomotor changes in the brain stem.

A 43-year-old man had typical recurrent attacks of ophthalmoplegic migraine. In his last attack he had in addition to the usual manifestation an iris hyperemia and circulating cells in the aqueous. Vessels with visible blood columns are encountered in the pupillary portion of the iris only when they are dilated, and cells in the aqueous are evidence of abnormal permeability of the ciliary body. Both phenomena occur only in inflammation of the anterior segment of the globe and in status dysraphicus with sympathetic heterochromia. In the author's patient, it seems probable that they were caused by transitory paresis of the vasomotor fibers. F. Herbert Haessler.

Cridland, Nigel. **The measurement of heterophoria.** Brit. Jour. Ophth., 1941, v. 25, April, pp. 141-166; and May, pp. 189-229.

Part one is divided into the following eight sections: position of the visual axes in orthophoria; anatomic position of rest; physiologic position of rest; possibility of falsifying the measurements; difficulties of wearing glasses for tests for heterophoria; heterophoria in relation to flying; tabulation of findings; summary of conclusions.

Part two includes four groups determining the fusion-free position. In group one dissociation is effected by limiting the field of vision of one or both eyes. Group two involves the test in which one image is displaced from the macula in such a manner as to make fusion impossible. Group three includes tests in which the stimulus to fusion is reduced or abolished by differentiation of the images seen by the two eyes, whether effected by change of color, form, or other characteristic of light incident. Group four explains the methods which do not attempt to suspend fusion.

Part three investigates the relative efficacy of the red-green and the Maddox-rod tests in revealing and measuring heterophoria. The first series of investigations was based upon 267 cases and an additional three series were concerned with further findings on further cases. The red-green tests were found unsatisfactory. Concerning the Maddox-rod test, the following conclusions are offered: (1) Suppression of the fusion tendency is good, and is increased by darkness. (2) The variability of the test is very small. (3) Care is essential to various points of detail, but is amply repaid by the consistency of results. (Bibliography of four pages.) D. F. Harbridge.

Goldberg, F. P. **Congenital paralysis of abduction with retraction of the eyeball.** Viestnik Opht., 1940, v. 17, pt. 6, p. 751.

A review of the literature and a tabulated report of 14 cases exhibiting the various motor anomalies characteristic of this syndrome. Ray K. Daily.

Goldberg, Sol. **Contact glasses as an aid in straightening the eyes.** Amer. Jour. Ophth., 1941, v. 24, Aug., p. 933.

Grigorieva, H. I. **Examination of convergence in various directions of fixation.** Viestnik Opht., 1940, v. 17, pt. 6, p. 781.

A total of 102 patients were tested on the Litinski apparatus. The results show that the near point of convergence recedes on looking up, and approaches the eyes on looking down. This variation should be kept in mind in the examination of aviators, and convergence should be tested in the upper and lower fields.

Ray K. Daily.

Machado, N. R. **Consideration of the treatment of strabismus.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 190-225.

In an article of 37 pages, the author urges the great importance of accurate and early correction of refractive errors, discusses the use of fusion exercises, and describes the principal muscle operations. (33 clinical and surgical illustrations, bibliography.)

W. H. Crisp.

Machado, Nicolino. **Treatment of strabismus.** Arquivos Brasileiros de Oft., 1941, v. 4, April, pp. 88-107.

A 19-page review of the subject, in Portuguese.

Semeraro, E. **Strabismus operation.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 176-179.

A technique for advancement, using a single suture which reconstructs the anatomic planes and advances the muscle at the same time, using a special forceps adapted for both fixation and suture. W. H. Crisp.

Silva, Linneu. **Medical treatment of strabismus.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 114-166.

This article of 53 pages deals with the subject under the following headings: general considerations, advisability of treatment, preliminary investigations, therapeutic plan, general methods of treatment, general treatment. The section on general methods of treatment deals with orthoptic training. (Bibliography, 8 illustrations.)

W. H. Crisp.

Sverdlick, José. **Surgery in functional strabismus.** Ophthalmos (Brazil), 1940, v. 2, no. 1, pp. 170-175.

A brief general discussion. (References.)

Torres Estrada, Antonio. **Treatment of strabismus.** Bol. del Hosp. Oft. de Ntra. Sra. de la Luz, 1941, v. 1, Jan.-Feb., pp. 170-196.

After description of his personal technique for advancement and lengthening, the author, in an article of 27 pages, recites briefly a number of illustrative cases, with surgical drawings and photographs of patients.

W. H. Crisp.

5

CONJUNCTIVA

Bartels, M., and Loens, M. **Questions on the causative agents of keratoconjunctivitis epidemica.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 83-84. (See Section 6, Cornea and sclera.)

Bertoldi, Maria. **Benign tubercle of the conjunctiva.** Rassegna Ital. d'Ottal., 1940, v. 9, May-June, pp. 380-391.

Because of the absence of glandular involvement, X-ray changes, cough, or any other evidence of tuberculosis, a tubercle occurring in the palpebral conjunctiva of a 13-year-old boy is reported as representing a "benign" form of tuberculosis. (One figure.)

Eugene M. Blake.

Castañe Decoud, D. D. de. **Histopathology of pterygium.** Anales Argentinos de Oft., 1941, v. 2, Jan.-Feb.-March, pp. 37-43.

A summary of the pathogenic theories and the general morphology of pterygium. The author promises later to present conclusions drawn from his own pathologic material. (4 illustrations.) W. H. Crisp.

Menshutin, M. A. **Prophylaxis of ophthalmia neonatorum.** Viestnik Opht., 1940, v. 17, pt. 6, p. 767.

A survey of the procedures current in various maternity homes. The conclusions are that 2-percent silver nitrate is more effective and no more irritating than 5-percent protargol.

Ray K. Daily.

Meves, Harald. **Is there a light etiology for vernal conjunctivitis?** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 86-91.

A girl 11 years old with vernal conjunctivitis also showed a light dermatosis of the uncovered parts of the skin. The progress of both affections was very similar, and protection from ultraviolet rays resulted in definite improvement. Gertrude S. Hausmann.

Muir, E. B. **Gonorrheal ophthalmia and gonorrheal ophthalmia neonatorum.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 879-894.

Puig Solanes, Magin. **Notes concerning ocular pemphigus and pseudopemphigus.** Anales de la Soc. Mexicana de Oft. y Oto-Rino-Laring., 1941, v. 16, Jan.-Feb., pp. 1-19.

The author describes three cases, one in a woman of 35 years, one in a woman of 75 years and a third in a woman of 55 years. In the first case the ocular disturbance began in the course of a general dermatosis characterized by bullae of various sizes and shapes distributed irregularly throughout the body as well as on the buccal mucous membrane. After subsidence of the acute general phenomena (including a febrile reaction), the ocular changes disappeared almost entirely, the patient continuing for nine months with a slight sensation of a foreign body and a slight mucous secretion. Beyond that time there were a series of outbreaks of the ocular disorder, of 10 or 12 days

duration, separated by periods of some weeks during which redness, burning, and the sensation of a foreign body continued. During each acute relapse, the vision fell noticeably. There were many cicatricial bands in the cul de sac, and the lower three tenths of the cornea in the right eye showed an incomplete ring of opacities.

In the second case the patient's chief complaint was a gradual loss of vision for the previous nine years, without inflammation of the anterior segment.

The third patient had experienced in the course of 24 years a continuous disturbance of the right eye, without exacerbation or remission, and characterized by pain, photophobia, lacrimation, and mucous secretion, with gradual reduction in visual acuity. The left eye had been disturbed for six years, without effect on the visual acuity. (Bibliography.) W. H. Crisp.

Reca, A. B. **Sulfanilamide in the treatment of trachoma.** Anales Argentinos de Oft., 1940, v. 1, Oct.-Nov.-Dec., pp. 426-429.

On the basis of 34 cases of trachoma at various stages, and of 8 miscellaneous cases of conjunctivitis of a chronic character, the author presents the following conclusions: Sulfanilamide is by no means a specific for trachoma. It appears to act chiefly in causing disappearance of burning, photophobia, and conjunctival secretion. It seems to aid involution of the corneal phenomena. W. H. Crisp.

Rollemberg Sampaio, J. M. **Abortive or dubious trachoma, suspect conjunctivitis?** Arquivos Brasileiros de Oft., 1941, v. 4, June, pp. 126-127.

The group of cases in which the author is disposed to make a doubtful diagnosis of trachoma, subject to later behavior of the eyes, is marked by the following symptoms: The conjunctiva of the everted upper lid is red but generally smooth. The upper cul de sac has some hard follicles. The bulbar conjunctiva is uniformly congested, the pericorneal vessels encroaching a little on to the limbus everywhere, and giving above at times the impression of a true "pannus tenuis." Among children a common sign is exaggerated blinking. W. H. Crisp.

Rubino, A., and Simonelli, M. **Vitamin P.P. (nicotinic acid) in vernal catarrh.** Rassegna Ital. d'Ottal., 1940, v. 9, May-June, pp. 332-336.

Twelve cases of vernal catarrh, four of aggravated form, were treated by oral or parenteral administration of vitamin P.P. The dose by mouth was 60 to 80 centigrams of the amide or 30 centigrams of nicotinic acid. The intramuscular dose was 20 centrigrams of the amide. Subjective symptoms improved rapidly, and vegetations were either greatly reduced or entirely cleared up. The report is only preliminary, but is most encouraging and the authors feel that it supports the theory of the photodynamic origin of the disease. Eugene M. Blake.

Savin, L. H. **Tarsectomy for trachoma, its indications, difficulties, and results.** Trans. Ophth. Soc. United Kingdom, 1940, v. 60, p. 163.

After removal of the hypertrophic tarsal plates, which are a source of mechanical irritation and a nidus for the infective virus, the disease in the residual conjunctiva clears rapidly, conjunctival discharge ceases, and the patient is rendered noninfectious. The operation is less trying than many mechanical and caustic treatments. The author's technique is outlined and final

results are given. Complications occurred in 7 of the 92 lids operated upon. Beulah Cushman.

Solares, Amiceto. **Keratoconjunctival lesions observed at high altitudes in Bolivia.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 900-913.

Stone, J. B., and Courtney, R. H. **Xerophthalmia and keratomalacia associated with obstructive biliary cirrhosis.** Virginia Med. Monthly, 1941, v. 68, March, p. 159. (See Section 6, Cornea and sclera.)

Tertsch, R. **The therapy of keratoconjunctivitis epidemica.** Klin. M. f. Augenh., 1941, v. 106., Jan., pp. 84-86. (See Section 6, Cornea and sclera.)

Valle, Sergio. **Diagnosis of trachoma.** Arquivos Brasileiros de Oft., 1941, v. 4, Feb., pp. 1-15.

A general discussion of the difficulties of such diagnosis, with references to the literature and emphasis upon the presence of corneal changes. The author states that in the Penido Burnier Institute (Brazil) systematic examination with the slitlamp, in patients complaining of symptoms commonly related to the conjunctiva and cornea, indicates a higher percentage of trachoma than that shown by the best statistics. W. H. Crisp.

6

CORNEA AND SCLERA

Aires, Francisco. **The operation of corneal grafting.** Arquivos Brasileiros de Oft., 1941, v. 4, Feb., pp. 26-50.

The author describes the technique of Elschnig, Filatov, Thomas, Castroviejo, and Wiener, with reproductions of illustrations by these authors. Operative indications and complications are reviewed. (Bibliography of 60 references.) W. H. Crisp.

Barkhash, S. A. **The placenta as plastic material in ocular surgery.** Viestnik Opht., 1940, v. 17, pt. 6, p. 758. (See Section 14, Eyelids and lacrimal apparatus.)

Bartels, M., and Loens, M. **Questions on the causative agents of keratoconjunctivitis epidemica.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 83-84.

In reference to the finding of diphtheroid bacilli in the epidemic of 1938 to 1940, the fact is mentioned that in a similar epidemic in 1938 xerosis bacteria were found. In the epidemic of 1938 to 1940 the keratoconjunctivitis was followed by a keratitis nummularis. Gertrude S. Hausmann.

Bursuk, G. G. **A distinctive type of senile corneal degeneration.** Viestnik Opht., 1940, v. 17, pt. 6, p. 799.

In the middle corneal layers of six patients, Bursuk found symmetrical opacities which caused the patients to complain of foggy vision. Bursuk believes that these were parenchymatous degenerations similar to gerontoxon. Ray K. Daily.

Corser, J. B. **Recurring superficial ulcerative keratitis.** Pennsylvania Med. Jour., 1941, v. 44, June, p. 1152.

The author reports six cases to show that, clinically, the withdrawal of certain foods from the diet has given most satisfactory results in preventing repetition of attacks. Theodore M. Shapira.

Fazakas, Alexander. **Fungus diseases of the cornea.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 56-63.

Different forms of aspergilli were

found in very increased numbers in inflamed eyes. Aspergilli, penicillia, actinomyces, and related groups of fungi were found to cause different forms of corneal infiltrations and sometimes corneal ulcers. One case of corneal ulcer led to an occlusion of the chamber angle by fungus growth, and subsequent increase of tension.

Gertrude S. Hausmann.

Kayser, B. **Assumed relations between macrocornea and hydrophthalmos and lack of their proof.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 63-69.

Megalocornea has no direct relation to hydrophthalmos. One form of secondary megalocornea occurs in cases of arrested hydrophthalmos.

Gertrude S. Hausmann.

Kopp, I. F. **Subconjunctival implantation of corneal tissue in the treatment of keratitis.** Viestnik Opht., 1940, v. 17, pt. 6, p. 708.

A piece of preserved cadaver cornea is implanted under the conjunctiva above the cornea. The results of 75 operations in various types of keratitis have convinced the author of the therapeutic effectiveness of the procedure. He believes that the biological processes taking place in the implant have a desensitizing effect and free the cornea of allergic tendencies.

Ray K. Daily.

Miklos, A. **Contributions to the studies of megalocornea in connection with sporadic megalocornea globosa.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 69-78.

Megalocornea and hydrophthalmos are two distinct diseases. A case of megalocornea globosa is described in which a cataract was extracted. The lens in these cases is usually subluxated, the tension on the zonular fibers being very strong. A conjunctival flap does not close the incision securely after extraction as the cornea collapses. Corneal sutures are advisable. (4 illustrations.) Gertrude S. Hausmann.

Skorodinskaja, V. V. **Therapeutic corneal transplantation in keratitis.** Viestnik Opht., 1940, v. 17, pt. 6, p. 699.

The rationale of this procedure is based on the author's belief that the transplanted cornea stimulates corneal metabolism and its defensive activities. The transplant was in all cases cadaver cornea preserved on ice. The corneal lesions were parenchymatous keratitis, luetic and tuberculous, sclerosing keratitis, and acne rosacea. (Illustrations.)

Ray K. Daily.

Solares, Amiceto. **Keratoconjunctival lesions observed at high altitudes in Bolivia.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 900-913.

Stone, J. B., and Courtney, R. H. **Xerophthalmia and keratomalacia associated with obstructive biliary cirrhosis.** Virginia Med. Monthly, 1941, v. 68, March, p. 159.

In this case, the authors believe that the absence or deficiency of bile in the gastro-intestinal tract had interfered with the normal digestion of fats, thus preventing the absorption of vitamin A to such a degree as to bring about the keratomalacia and xerophthalmia.

Theodore M. Shapira.

Tertsch, R. **The therapy of keratoconjunctivitis epidemica.** Klin. M. f. Augenh., 1941, v. 106, Jan., pp. 84-86.

Touching the lids with a 0.25 to 0.5-percent silver-nitrate solution and careful washing of the lids afterwards gave the best results in treating keratocon-

junctivitis epidemica. Paraffin oil was instilled in the conjunctival sac after treatment. Between treatments 3-percent boric acid and a weak oxycyanide solution were used.

Gertrude S. Hausmann.

Thomas and Weill. **A case of ocular and cutaneous tuberculosis treated by Rubrophen.** Bull. Soc. d'Opht. de Paris, 1939, April, p. 322.

A 40-year-old woman with parenchymatous keratitis and lupus erythematosus of the nose and hand was treated by Rubrophen, locally and intravenously. The authors credit this treatment for the prompt subsidence of the lesions. George A. Filmer.

Viswalingam, A. **Epidemic superficial punctate keratitis in Malaya.** Brit. Jour. Ophth., 1941, v. 25, July, pp. 313-324.

The discussion is based on 3,521 cases occurring in epidemic form over a three year period (1935 to 1938). The question of differentiating superficial punctate keratitis from simple conjunctivitis and from herpes febrilis is discussed, the onset and symptoms of the disease being presented in detail. Etiology of the ailment is obscure, smears and bacteriologic examination of some 355 fresh cases being negative. The disease was found not to be confined to any special race, class, or age. Findings of the author lead to the belief that the disease is caused by an exogenous infection, the agent probably being a virus of considerable toxicity.

When seen early, response to treatment by the usual hygienic and curative procedures was satisfactory. Hot applications, warm irrigations, the use of argyrol or protargol in drops followed by weak yellow-oxide-of-mercury ointment usually sufficed. In cases seen late, treatment depended upon the complications which had arisen, each complication requiring a specific treatment. (Figures, plates, tables, references.) D. F. Harbridge.

7

UVEAL TRACT, SYMPATHETIC DISEASE, AND AQUEOUS HUMOR

Krasnoretzki, P. A., and Lotin, A. V. **A case of spontaneous iris cyst.** Viestnik Opht., 1940, v. 17, pt. 6, p. 796.

A man 32 years old developed a cyst of the iris which filled one third of the anterior chamber and reduced vision to 4/10. The cyst was excised and the diagnosis confirmed microscopically. (Illustrations.) Ray K. Daily.

Letchworth, T. W. **A case of cyclitis of 24-years standing cured by tonsillectomy.** Trans. Ophth. Soc. United Kingdom, 1940, v. 60, p. 155.

The patient had experienced the first symptoms at the age of 25 years, at which time the tonsils had been considered negative by several examiners. When again seen by Letchworth, 24 years later, a culture from the nasopharnyx was positive for streptococcus viridans, and subsequently the tonsils were removed. Desensitization to the streptococcus viridans was carried out. About one year later for the first time the anterior chamber was free of cells and precipitates. Beulah Cushman.

8

GLAUCOMA AND OCULAR TENSION

Radzikhovski, B. L. **Maklakov's new tonometer.** Viestnik Opht., 1940, v. 17, pt. 6, p. 765.

A description of the instrument. (Illustration.) Ray K. Daily.

Sanchez Bulnes, Luis. **A new technique in the treatment of glaucoma (anterior combined cyclodialysis).** Anales de la Soc. Mexicana de Oft. y Oto-Rino-Laring., 1941, v. 16, Jan.-Feb., pp. 33-35.

A limbal incision is made beneath a square conjunctival flap which has a suture. Cyclodialysis from the angle of the anterior chamber backward is followed by use of the scleral punch, iridectomy, and tying of the conjunctival suture. W. H. Crisp.

Sugar, H. S. **The mechanical factors in the etiology of acute glaucoma.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 851-872.

Torres Estrada, A. **Cataract and acute inflammatory glaucoma.** Bol. del Hosp. Oft. de Ntra. Sra. de la Luz, 1940, v. 1, Sept.-Dec., pp. 133-147.

Having accidentally injured the lens capsule while doing an iridectomy for acute glaucoma complicating hypermature cataract, the author removed the milky contents of the capsule and then extracted the capsule itself. Since then he has continued to extract cataracts in eyes whose condition was complicated by acute glaucoma arising from changes in the cataract, such as hypermaturity or subluxation. Three cases are described. W. H. Crisp.

9

CRYSTALLINE LENS

Berens, Conrad. **Capsulotomy and iridocapsulotomy.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 915-919.

Blanchi, Guido. **Dinitrophenol cataract.** Rassegna Ital. d'Ottal., 1941, v. 9, July-Aug. pp. 493-523.

The pharmacologic action of dinitrophenol and its effect upon the ocular tissues are discussed. Experiments on animals are related, and three cases of cataract due to the drug are described. The etiology of such cataracts is attributed to the increased permeability of the capsule, resulting from the toxic products originating in damage to the liver and kidneys. (Review of the literature.) Eugene M. Blake.

Burleson, J. H., and McCurdy, M. W. **Is operation for senile cataract on an ambulatory patient justifiable?** Texas State Jour. Med., 1941, v. 36, Feb., p. 680.

The authors relate their experiences in allowing patients to leave the hospital four hours after a cataract extraction. They believe the ambulatory method is feasible when circumstances make it necessary.

Theodore M. Shapira.

Crisp, W. H. **The occasional operator.** Ophth. Ibero Amer., 1940, v. 2, no. 1, pp. 1-6.

For the cataract operation emphasis is laid on exact timing of the steps of anesthesia, including preliminary instillation of cocaine and adrenalin, akinesia, retrobulbar injection, and a small injection of cocaine and adrenalin above and below the cornea, followed by a five-minute interval before making the incision. With such anesthesia, deliberate and unhurried action is permissible for most steps of the operation. W. H. Crisp.

Gandolfi, G. **Proteolytic activity of normal and cataractous lenses.** Rassegna Ital. d'Ottal., 1940, v. 9, Nov.-Dec., pp. 702-707.

Lenses removed within the capsule were employed by the author in his studies of proteolytic activity. He

concludes that the cataractous lens possesses a proteolytic power not encountered in the normal lens. The report confirms previous findings.

Eugene M. Blake.

Jona, Sergio. **Postoperative separation of the choroid.** Rassegna Ital. d'Ottal., 1940, v. 9, Sept.-Oct., pp. 553-577.

Jona describes three cases of separation of the choroid, one following an intracapsular cataract extraction, one an extracapsular extraction, and one a Lagrange operation. He discusses the theories which attempt to explain the cause of this condition, and reviews the literature, but offers nothing new. (4 figures.) Eugene M. Blake.

Mattos, W. B. **Twenty years of cataract surgery.** Arquivos Brasileiros de Oft., 1940, v. 3, Dec., pp. 295-301.

Briefly but discursively reminiscent.

Petronio, G. **An unusual cataract—sutural and zonular.** Rassegna Ital. d'Ottal., 1940, v. 9, May-June, pp. 325-331.

A 14-year-old girl presented an unusual type of congenital cataract. There was an intensely white nuclear and perinuclear opacity, heart-shaped in form. In this opacity the anterior embryonal suture was strongly outlined. Extending from the perinuclear opacity were 12 clearly defined riders which penetrated the perfectly clear periphery. In the author's opinion, an embryonal suture cataract had been superimposed upon a zonular cataract. (One figure.) Eugene M. Blake.

Torres Estrada, A. **Cataract and acute inflammatory glaucoma.** Bol. del Hosp. Oft. de Ntra. Sra. de la Luz, 1940, v. 1, Sept.-Dec., pp. 133-147. (See Section 8, Glaucoma and ocular tension.)

Vail, Derrick. **On the mechanism and causes of hyphema after cataract extraction.** Amer. Jour. Ophth., 1941, v. 24, Aug., pp. 920-927.

10

RETINA AND VITREOUS

Agundis, Teodulo. **Clinical history of the child M.S.M. (Familial amaurotic idiocy).** Anales de la Soc. Mexicana de Oft. y Oto-Rino-Laring., 1941, v. 16, Jan.-Feb., pp. 25-33.

The Mexican parents were second cousins. Both parents had probably had syphilis. W. H. Crisp.

Angius, Tullio. **Retinal hemorrhage in internal leishmaniosis.** Rassegna Ital. d'Ottal., 1940, v. 9, May-June, pp. 365-379.

A 16-year-old boy presented the usual findings of the internal form of leishmaniosis. He developed numerous punctiform hemorrhages arranged along the vessels in the whole periphery of the left retina. There was a pale disc, peripapillary edema, and a central macular hemorrhage, all of which cleared up under treatment of the systemic disease. The literature is fully reviewed. Eugene M. Blake.

Arndt, E. W. **Infection of sphenoidal sinuses with secondary infection of the eyes.** Brit. Jour. Ophth., 1941, v. 25, July, pp. 324-330.

Arndt reports two cases of special interest, a detachment of the retina in each eye having taken place in the one, and an acute optic neuritis of one eye in the other. The first patient was a physician's wife, 32 years of age, and the other a single woman 28 years of age. In both cases the infection of the

sphenoidal sinuses apparently resulted from mild attacks of influenza. In neither case was there a frank suppuration, there being instead a deep congestion, with only a mere bead of pus showing on one side in the one case. Detachment of the retina is rare in septic cases. It was thought that an ultra-short-wave treatment in the case reported here might have a bad effect on the retinas. Perfect reposition of the retinas, with recovery of vision, was brought about by complete rest in a semi-recumbent position. In optic neuritis, it is the experience of the author that when the exact cause cannot be found and the case does not respond to treatment, an ample "bloodletting" from a high operation in the nose brings about the desired results. (Field charts.) D. F. Harbridge.

Borsello, G., and Brunetti, F. **The vestibulo-retinal reflex.** Rassegna Ital. d'Ottal., 1940, v. 9, Sept.-Oct., pp. 606-625.

The authors have demonstrated that caloric and mechanical excitation of the vestibular system is followed by a depressor reaction of the central retinal artery. This is manifested by a characteristic modality of definite constancy sufficient to assert the existence of a true vestibulo-retinal reflex.

Eugene M. Blake.

Lijo Pavia, J. **Detachment of the retina; remote results of surgical treatment.** La Semana Med., 1941, v. 48, July 24, pp. 211-222.

For reporting cures, the author postulates recovery of at least 1/10 of vision, or reattachment of the retina and increase of visual field. On the latter basis he claims 65 percent of surgical cures in his own 60 cases. Vision of 2/3 to 1.0 was obtained in six cases; of 1/3 to 1/2 in six cases; of 2/10 to 1/20 in 25; vision of less than 1/20, but with some improvement, in two cases. The technique is discussed. (34 references, illustrations.)

W. H. Crisp.

Meyer, I. C. **Angioid streaks of the retina.** Arquivos Brasileiros de Oft., 1941, v. 4, April, pp. 75-88.

A single case report is accompanied by a rather extensive discussion of the literature. The patient, a man of 41 years, had a history of syphilis, and had been under treatment for several months for chronic nephritis. In each eye the peripapillary area had lost its pigment, although the retinal vessels were normal. Each eye, but especially the left, presented a group of branching striae in the paracentral area. (2 fundus illustrations in color.)

W. H. Crisp.

NEWS ITEMS

Edited by Dr. Ralph H. Miller, 803 Carew Tower, Cincinnati

News items should reach the editor by the twelfth of the month

Deaths

Dr. George E. Bellows, Laguna Beach, California, died June 19, 1941, aged 79 years.

Dr. Burton Haseltine, Chicago, Illinois, died July 12, 1941, aged 66 years.

Dr. Joseph T. Abshire, Kaplan, Louisiana, died June 22, 1941, aged 72 years.

Dr. Howard Murray Ritter, Williamsport, Pennsylvania, died June 1, 1941, aged 71 years.

Dr. Thomas Earl Goyer, Jackson, Tennessee, died June 16, 1941, aged 53 years.

Dr. Amos Morris Peters, Alexandria, Louisiana, died June 19, 1941, aged 63 years.

Dr. Tyrus Eugene Swan, Easton, Pennsylvania, died May 28, 1941, aged 79 years.

Dr. Edmund S. Ferguson, Oklahoma City, Oklahoma, died June 28, 1941, aged 70 years.

Dr. John Bell, New Glasgow, Nova Scotia, Canada, died May 27, 1941, aged 65 years.

Dr. Ernest Franz Berne, Indiana, died June 27, 1941, aged 76 years.

Dr. Felton D. Watts, Portland, Oregon, died June 17, 1941, aged 75 years.

Dr. John J. Johnson, Harrison, Arkansas, died in June, 1941, aged 80 years.

Dr. Lee Cone Van Wagner, New Berlin, New York, died June 18, 1941, aged 71 years.

Dr. John M. Tracy, Springfield, Massachusetts, died July 8, 1941, aged 72 years.

Dr. Abner R. Renninger, Philadelphia, Pennsylvania, died July 25, 1941, aged 65 years.

Dr. Herman Harvey Sanderson, Detroit, Michigan, died July 1, 1941, aged 71 years.

Dr. William L. Case, New York, New York, died July 3, 1941, aged 71 years.

Dr. John W. Duncan, Jourdantown, Texas, died May 11, 1941, aged 67 years.

Dr. Thomas Francis Conroy, Sr., Palo Alto, California, died July 6, 1941, aged 76 years.

Dr. William Bernhart Hamaker, Lancaster, Pennsylvania, died July 15, 1941, aged 63 years.

Dr. Eustace Cosmo Mason, Quebeck, Tennessee, died July 15, 1941, aged 72 years.

Dr. Lawrence N. Breene, Farrell, Pennsylvania, died July 19, 1941, aged 54 years.

Dr. Hiram Leslie Reckard, Baltimore, Maryland, died July 26, 1941, aged 69 years.

Dr. Thomas A. O'Brien, Philadelphia, Pennsylvania, died June 21, 1941, at his summer home in Ship Bottom, New Jersey, aged 58 years.

Miscellaneous

The thirty-first annual Clinical Congress of the American College of Surgeons will be held at the Statler Hotel and The Copley-Plaza in Boston, November 3 to 7, 1941. A number of operative and dry clinics of interest to ophthalmologists will be given during the days of the meeting. A symposium on "Surgery of heterophoria and heterotropia" is planned for Tuesday evening, November 4th. The following will participate: Dr. James W. White, New York; Dr. Derrick Vail, Cincinnati; Dr. Edwin B. Dunphy, Boston; and Dr. William Thornwall Davis, Washington, D.C.

In addition to the formal part of the program there will be a series of round-table conferences on the following subjects: Surgery of squint; Surgery of the tear passages; and Surgery of the orbit.

The Eye Conservation Division of the Cleveland Safety Council presented a program, on September 24th, based on the problem of eye hazards in industry due to the increase in production for defense. Dr. Howell L. Begle of Detroit, Michigan, spoke on "Visual needs in industry and in war." Dr. Albert D. Frost of Columbus, Ohio, lectured on "The care of industrial eye injuries." Dr. P. G. Moore, of Cleveland, Ohio, discussed "The end results of eye injuries." Mr. Milton Bowman, recently appointed Regional Safety Consultant for the National Committee for the Conservation of Manpower in Defense Industries, lectured on "The importance of eye conservation in defense industries."

The Chicago Eye, Ear, Nose, and Throat College announces its ninth annual Fall Course in "Surgery of the eye and adnexa," from November 3 to 8, 1941, inclusive. The program includes the following lecturers: Dr. Ephraim K. Findlay, Dr. William W. Gailey, Dr. Michael Goldenburg, Dr. L. Robert Mellin, Dr. Earl D. Merz, Dr. Oscar B. Nugent, Dr. Dwight C. Orcutt, Dr. Albert G. Peters, Dr. Joseph E. Schaefer, Dr. Carl Wagner, Dr. Sydney Walker, Jr., Dr. Fay M. Whitsell, and Dr. George H. Woodruff.

The Inter-State Postgraduate Medical Association of North America announces that its International Medical Assembly will be held in the Public Auditorium of Minneapolis, Minnesota, October 13th to 17th, inclusive.

The report of the National Society for the Prevention of Blindness, Inc., Great Britain, is the twenty-sixth of that organization. Subjects stressed are: the increase of eye hazards with the increase of industrial production, a subject of scientific interest to both Britain and America; the society's glaucoma exhibit at the American Medical Association; the evaluation of vision-testing procedures; preventable blindness due to venereal diseases, and inclusion of the subject of conservation of sight in the education of nurses.

Societies

The Kansas City Society of Ophthalmology and Otolaryngology has arranged an excellent program for the year 1941-1942. Arrangements have been made to present guest speakers of national distinction at the various meetings. Officers for the year are: Dr. Joseph W. McKee, president; Dr. LaVerne B. Spake, first vice-president; Dr. Wayne B. Granger, second vice-president; Dr. W. E. Keith, secretary; and Dr. Edgar W. Johnson, treasurer.

Personals

A dinner was given in honor of Dr. John E. Weeks on the occasion of the centennial of the College of Medicine of New York University on Monday, October 6, 1941, at the Union Club, New York City.

Dr. Edward Jackson, Denver, presented a paper on "Expanding medicine" at the dedication of the Hurst Eye, Ear, Nose, and Throat Hospital, Longview, Texas, July 5, 1941.

Dr. C. Dwight Townes has recently been appointed Chairman of the Department of Ophthalmology and Clinical Professor of Ophthalmology at the University of Louisville School of Medicine.

The honorary degree of Doctor of Science was awarded to Dr. William P. Wherry of Omaha by Wayne University of Detroit, Michigan, in June, 1941.

The National League for Prevention of Blindness in Brazil awarded its national prize to Dr. Isaias Alves of São Salvador.

Miss Ida Mann has been appointed Margaret Ogilvie Reader in Ophthalmology beginning October 1, 1941, at the University of Oxford (England).